Supporting Information

Synthesis of new chiral lactam–fused pyridine derivatives

Tetsuya Sengoku,[a] Yusuke Murata,[b] Chihiro Suzuki,[a] Masaki Takahashi[a] and Hidemi Yoda*[a,b]

[a]*Department of Applied Chemistry, Faculty of Engineering, Shizuoka University, 3–5–1 Johoku, Naka–ku, Hamamatsu 432–8561, Japan.*

[b]*Graduate School of Science and Technology, Shizuoka University, 3–5–1 Johoku, Naka–ku, Hamamatsu 432–8561, Japan.*

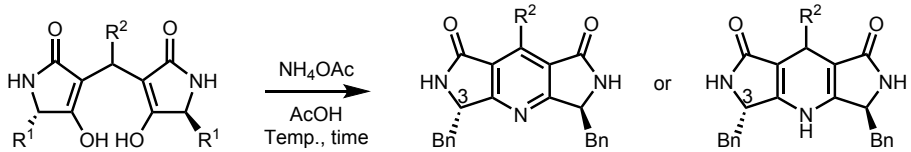
E–mail: tchyoda@ipc.shizuoka.ac.jp

The following data are included in this material:

General methods:

All solvents and reagents were of reagent grade quality from Wako Pure Chemicals and Tokyo Chemical Industry (TCI), and used without further purification. Methanol (MeOH) was dried over MS3Å prior to use. Phenylalanine-derived tetramic acid,[1] leucine-derived tetramic acid,[2] enamines **6a**,[3] **6b**,[4] **6c**,[5] and **6d**[6] were synthesized according to the literature. All new compounds were characterized by NMR, IR, and elemental analysis. The ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra operating at the frequencies of 300 and 75 MHz, respectively, were recorded on a JEOL JNM–AL300 spectrometer in chloroform–*d* ($CDCl_3$) unless otherwise noted. Chemical shifts are reported in parts per million (ppm) relative to TMS and the solvent used as internal standards, and the coupling constants are reported in hertz (Hz). Optical rotations were measured in 1 dm path length cell of 2 mL capacity using a JASCO Model DIP–1000 polarimeter at a wavelength of 589 nm. Reactions were monitored by thin layer chromatography (TLC) using 0.25 mm Merck silica gel 60–F254 precoated silica gel plates by irradiation with UV light and/or by treatment with a solution of phosphomolybdic acid in EtOH followed by heating. Column chromatography was performed on Kanto Chemical silica gel 60N eluting with the indicated solvent system. Melting points were measured with a Yanaco MP–S3 micro melting point apparatus. Fourier transform infrared (FTIR) spectra were recorded on a JASCO FT/IR–550 spectrometer. Elemental analyses were performed by JSL Model JM 10 instruments.

Synthesis of C_2-symmetric lactam–fused pyridines 2 from chiral diols 1:



1a : R^1 = Bn, R^2 = H
b : R^1 = Bn, R^2 = Et
c : R^1 = Bn, R^2 = Ph

2a-c **3a-c**

Table S1. Reaction of chiral diols **1** with ammonium salts.

Entry	**1**	NH_4OAc [equiv.]	*T* [ºC]	*t* [h]	**2** ([%])	ratio[a] (**2** : *epi*-**2**)	**3** ([%])	ratio[a] (**3** : *meso*-**3**)
1	**1a**	1	r.t.	48	**2a** (0)	–	**3a** (0)	–
2	**1a**	1	100	11	**2a** (62)	53 : 47	**3a** (0)	–
3	**1b**	2	100	11	**2b** (<48)	66 : 34	**3b** (18)	–[b]
4	**1b**	50	100	1	**2b** (trace)	–	**3b** (62)	35 : 65
5	**1b**	50	90	1	**2b** (trace)	–	**3b** (53)	51 : 49
6	**1b**	50	80	1.5	**2b** (trace)	–	**3b** (46)	55 : 45
7	**1b**	50	70	3.5	**2b** (trace)	–	**3b** (60)	49 : 51
8	**1c**	50	100	1	**2c** (trace)	–	**3c** (43)	63 : 37
9	**1c**	50	70	9	**2c** (trace)	–	**3c** (44)	61 : 39

[a] Diastereomeric ratios were determined by ^{1}H NMR spectroscopy. [b] Not determined.

Characterization of 2c:

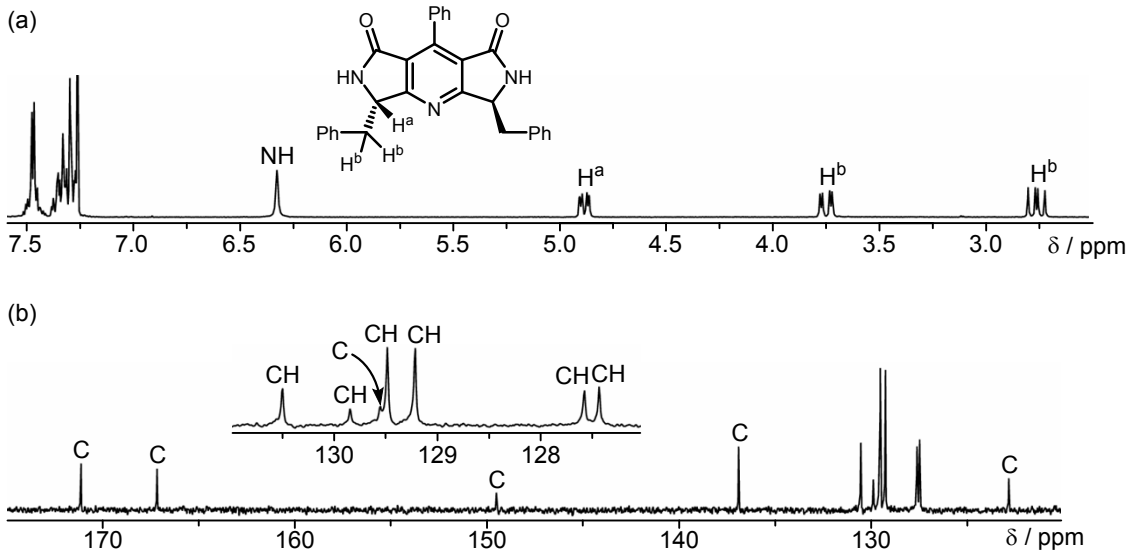


Figure S1. NMR spectra for **2c**. (a) ^{1}H NMR spectrum (300 MHz, $CDCl_3$, 2.5-7.6 ppm). (b) ^{13}C NMR spectrum (300 MHz, $CDCl_3$, 120-175 ppm). Multiplicities were assigned by DEPT experiment.

Experimental procedures and characterization data:

Synthesis and characterization of 4a[7]

To a solution of phenylalanine-derived tetramic acid (500 mg, 2.65 mmol) was added benzaldehyde (845 mg, 7.95 mmol) and *conc.* hydrochloric acid (10 drops) at room temperature. After stirring the mixture for 30 min, the resulting precipitate was filtered, washed with hexane and dried in vacuo to give **4a** (691 mg, 94%, major isomer/minor isomer = 4/1 in $CDCl_3$) as a yellow solid: R_f = 0.40 (silica gel, hexane/AcOEt = 1/1); M.p. 175–177 °C; $[\alpha]_D^{27}$ –334 (*c* 0.570, $CHCl_3$); IR (KBr) 3233 (N–H), 1687 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.46-8.42 (m, 2H, minor isomer, Ar*H*), 8.41-8.36 (m, 2H, major isomer, Ar*H*), 7.80 (s, 1H, minor isomer, C*H*), 7.79 (s, 1H, major isomer, C*H*), 7.62-7.44 (m, 3H, Ar*H*), 7.35-7.19 (m, 5H, Ar*H*), 6.60 (brs, 1H), 4.26 (dd, *J* = 3.6, 9.6 Hz, 1H, minor isomer, C*H*), 4.17 (dd, *J* = 3.6, 9.6 Hz, 1H, major isomer, C*H*), 3.32 (dd, *J* = 3.6, 13.8 Hz, 1H, CH_2), 2.79 (dd, *J* = 9.6, 13.8 Hz, 1H, minor isomer, CH_2), 2.78 (dd, *J* = 9.6, 13.8 Hz, 1H, major isomer, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.8 (*C*), 196.8 (*C*), 168.9 (*C*), 167.5 (*C*), 150.1 (*C*H), 149.2 (*C*H), 136.2 (*C*), 135.3 (*C*H), 134.0 (*C*H), 133.9 (*C*H), 133.5 (*C*H), 133.2 (*C*), 132.7 (*C*), 129.6 (*C*H), 129.09 (*C*H), 129.07 (*C*H), 128.99 (*C*H), 127.4 (*C*H), 123.9 (*C*), 123.4 (*C*), 62.5 (*C*H), 61.8 (*C*H), 38.8 (*C*H_2), 38.7 (*C*H_2). Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.90; H, 5.37; N, 5.07.

General procedure for the synthesis of benzylidene tetramic acids (4b-d)

All the experiments for the synthesis of benzylidene tetramic acids (**4b-d**) were carried out as described in the following typical procedure. For example, the reaction of phenylalanine-derived tetramic acid with *p*-tolualdehyde in the presence of hydrochloric acid for the synthesis of **4b** was exemplified as follows.

Synthesis and characterization of 4b

To a solution of phenylalanine-derived tetramic acid (199 mg, 1.05 mmol, 1.0 equiv.) and *p*-tolualdehyde (631 mg, 5.25 mmol, 5.0 equiv.) in EtOH (1.1 mL, 0.95 M for tetramic acid) was added *conc.* hydrochloric acid (5 drops) at room temperature. After stirring the solution for 17 h, the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica gel, hexane/AcOEt = 3/1 to 1/1) to give **4b** (268 mg, 88%, major isomer/minor isomer = 3/1 in $CDCl_3$) as a yellow solid: R_f = 0.40 (silica gel, hexane/AcOEt = 1/1); M.p. 158–160 °C; $[\alpha]_D^{25}$ –323 (*c* 0.625, $CHCl_3$); IR (KBr) 3182 (N–H), 3063 (N–H), 2917 (C–H), 1690 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, *J* = 7.8 Hz, 2H, minor isomer, Ar*H*), 8.29 (d, *J* = 8.4 Hz, 2H, major isomer, Ar*H*), 7.76 (brs, 1H, N*H*), 7.71 (s, 1H, minor isomer, C*H*), 7.66 (s, 1H, major isomer, C*H*), 7.30-7.14 (m, 7H, Ar*H*), 4.22 (dd, *J* = 3.9, 8.4 Hz, 1H, minor isomer, C*H*), 4.13 (dd, *J* = 3.9, 8.4 Hz, 1H, major isomer, C*H*), 3.25 (dd, *J* = 3.9, 14.1 Hz, 1H, CH_2), 2.84 (dd, *J* = 8.4, 14.1 Hz, 1H, CH_2), 2.42 (s, 3H,

major isomer, CH_3), 2.40 (s, 3H, minor isomer, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.0 (*C*), 197.0 (*C*), 169.4 (*C*), 167.9 (*C*), 149.7 (*C*H), 148.8 (*C*H), 145.3 (*C*), 144.7 (*C*), 136.2 (*C*), 135.4 (*C*H), 134.1 (*C*H), 130.8 (*C*), 130.1 (*C*), 129.8 (*C*H), 129.7 (*C*H), 129.6 (*C*H), 128.8 (*C*H), 127.1 (*C*H), 123.0 (*C*), 122.4 (*C*), 62.3 (*C*H), 61.7 (*C*H), 38.6 (*C*H_2), 38.5 (*C*H_2), 22.0 (*C*H_3), 21.9 (*C*H_3). Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88; N, 4.81. Found: C, 78.36; H, 5.77; N, 5.19.

Characterization for 4c

The crude product was purified by column chromatography (silica gel, hexane/AcOEt = 2/1) to give **4c** (293 mg, 91%, major isomer/minor isomer = 2/1 in $CDCl_3$) as a yellow solid: R_f = 0.29 (silica gel, hexane/AcOEt = 1/1); M.p. 130–132 °C; $[\alpha]_D^{27}$ –295 (*c* 0.665, $CHCl_3$); IR (KBr) 3180 (N–H), 3068 (N–H), 1681 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (d, *J* = 9.0 Hz, 2H, minor isomer, Ar*H*), 8.45 (d, *J* = 8.4 Hz, 2H, major isomer, Ar*H*), 7.69 (s, 1H, minor isomer, C*H*), 7.65 (s, 1H, major isomer, C*H*), 7.48 (brs, 1H, N*H*), 7.28-7.15 (m, 5H, Ar*H*), 6.98 (d, *J* = 9.0 Hz, 2H, major isomer, Ar*H*), 6.93 (d, *J* = 9.0 Hz, 2H, minor isomer, Ar*H*), 4.21 (dd, *J* = 3.9, 8.4 Hz, 1H, minor isomer, C*H*), 4.13 (dd, *J* = 3.9, 8.7 Hz, 1H, major isomer, C*H*), 3.87 (s, 3H, major isomer, CH_3), 3.86 (s, 3H, minor isomer, CH_3), 3.27 (m, 1H, CH_2), 2.82 (m, 1H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.1 (*C*), 197.0 (*C*), 169.8 (*C*), 168.4 (*C*), 164.5 (*C*), 164.1 (*C*), 149.5 (*C*H), 148.6 (*C*H), 138.2 (*C*H), 136.9 (*C*H), 136.4 (*C*), 129.5 (*C*H), 128.9 (*C*H), 127.1 (*C*H), 126.7 (*C*), 125.9 (*C*), 121.2 (*C*), 120.5 (*C*), 114.5 (*C*H), 62.4 (*C*H), 61.6 (*C*H),

55.61 (*C*H_3), 55.56 (*C*H_3), 38.8 (*C*H_2), 38.6 (*C*H_2). Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 74.08; H, 5.52; N, 4.60.

Characterization for 4d

The crude product was purified by column chromatography (silica gel, hexane/AcOEt = 4/1 to 3/1) to give **4d** (256 mg, 62%, major isomer/minor isomer = 1.1/1 in $CDCl_3$) as a yellow solid: R_f = 0.46 (silica gel, hexane/AcOEt = 1/1); M.p. 150–152 °C; $[\alpha]_D^{24}$ –53.7 (*c* 1.24, $CHCl_3$); IR (KBr) 3190 (N–H), 3070 (N–H), 2954 (C–H), 2869 (C–H), 1687 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (brs, 1H, minor isomer, N*H*), 8.51-8.48 (m, 2H, minor isomer, Ar*H*), 8.41-8.37 (m, 2H, major isomer, Ar*H*), 8.37 (brs, 1H, major isomer, N*H*), 7.81 (s, 1H, major isomer, C*H*), 7.79 (s, 1H, minor isomer, C*H*), 7.59-7.43 (m, 3H, Ar*H*), 4.09 (dd, *J* = 4.2, 9.6 Hz, 1H, minor isomer, C*H*), 4.00 (dd, *J* = 4.2, 9.6 Hz, 1H, major isomer, C*H*), 1.93 (m, 1H, C*H*), 1.76 (m, 1H, CH_2), 1.55 (m, 1H, CH_2), 1.04-0.98 (m, 6H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.4 (*C*), 198.5 (*C*), 169.6 (*C*), 168.5 (*C*), 149.5 (*C*H), 148.6 (*C*H), 135.2 (*C*H), 133.8 (*C*H), 133.7 (*C*H), 133.31 (*C*), 133.27 (*C*H), 132.8 (*C*), 129.0 (*C*H), 128.8 (*C*H), 124.1 (*C*), 123.6 (*C*), 60.1 (*C*H), 59.3 (*C*H), 41.7 (*C*H_2), 41.6 (*C*H_2), 25.0 (*C*H), 24.9 (*C*H), 23.5 (*C*H_3), 23.4 (*C*H_3), 21.6 (*C*H_3), 21.5 (*C*H_3). Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.87; H, 6.91; N, 5.87.

Synthesis and characterization of 5a[8]

To a solution of phenylalanine-derived tetramic acid (550 mg, 2.91 mmol) in MeOH/EtOH (1/1, 15 mL) was added ammonium acetate (2.24 g, 29.1 mmol) at room temperature. After stirring the reaction mixture for 24 h, the solvent was removed under reduced pressure. The residue was dissolved in saturated $NaHCO_3$ aq. (10 mL), extracted with dichloromethane (70 mL×15), dried over Na_2SO_4, filtered, and concentrated in vacuo to give **5a** (295 mg, 54%) as a pale brown solid: R_f = 0.29 (silica gel, $CHCl_3$/MeOH = 10/1); M.p. 199–200 °C; $[\alpha]_D^{27}$ –61.6 (*c* 0.515, MeOH); IR (KBr) 3362 (N–H), 3177 (N–H), 2960 (C–H), 1627 (C=O) cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 7.29-7.17 (m, 5H, Ar*H*), 4.55 (s, 1H, C*H*), 4.28 (dd, *J* = 4.2, 7.2 Hz, 1H, C*H*), 3.17 (dd, *J* = 4.2, 13.8 Hz, 1H, CH_2), 2.78 (dd, *J* = 7.2, 13.8 Hz, 1H, CH_2); ^{13}C NMR (75 MHz, CD_3OD) δ 180.5 (*C*), 170.3 (*C*), 138.1 (*C*), 131.0 (*C*H), 129.5 (*C*H), 128.0 (*C*H), 89.1 (*C*H), 60.2 (*C*H), 40.1 (*C*H_2). Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.24; H, 6.53; N, 14.83.

Synthesis and characterization of 5b[8]

To a solution of leucine-derived tetramic acid (285 mg, 1.84 mmol) in MeOH/EtOH (1/1, 9.2 mL) was added ammonium acetate (1.42 g, 18.4 mmol) at room temperature. After stirring the reaction mixture for 29 h, the solvent was removed under reduced pressure. The residue was dissolved in saturated $NaHCO_3$ aq. (10 mL), extracted with dichloromethane (30 mL×20), dried over Na_2SO_4, filtered, and

concentrated in vacuo to give **5b** (120 mg, 42%) as a pale yellow solid: R_f = 0.29 (silica gel, $CHCl_3$/MeOH = 10/1); M.p. 191–193 °C; $[\alpha]_D^{27}$ –35.3 (*c* 0.560, MeOH); IR (KBr) 3201 (N–H), 2957 (C–H), 1627 (C=O) cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 4.61 (s, 1H, C*H*), 4.07 (dd, *J* = 3.3, 9.9 Hz, 1H, C*H*), 1.80 (m, 1H, C*H*), 1.62 (ddd, *J* = 3.3, 9.9, 13.5 Hz, 1H, CH_2), 1.38 (ddd, *J* = 3.3, 9.9, 13.5 Hz, 1H, CH_2), 0.99 (d, *J* = 6.3 Hz, 3H, CH_3), 0.97 (d, *J* = 6.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, CD_3OD) δ 180.8 (*C*), 172.1 (*C*), 88.1 (*C*H), 58.1 (*C*H), 44.1 (*C*H_2), 26.4 (*C*H), 24.5 (*C*H_3), 22.0 (*C*H_3). Anal. Calcd for $C_8H_{14}N_2O$: C, 62.31; H, 9.15; N, 18.17. Found: C, 62.41; H, 9.16; N, 18.06.

General procedure for the synthesis of lactam–fused pyridines.

All the experiments for the synthesis of lactam–fused pyridines were carried out as described in the following typical procedure. For example, the reaction of **4a** with **5a** for the synthesis of **2c** was exemplified as follows.

Synthesis and characterization of 2c

To a solution of **4a** (35.6 mg, 0.128 mmol, 1.5 equiv.) and **5a** (16.1 mg, 0.0855 mmol, 1.0 equiv.) in MeOH (0.85 mL, 0.1 M for **5a**) was added citric acid (8.2 mg, 0.043 mmol, 0.5 equiv.) at room temperature under a nitrogen atmosphere. After stirring the solution at reflux for 6 h, the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica gel,

$CHCl_3$/MeOH = 20/1 to 10/1) to give a diastereomeric mixture of dihydropyridines (41.4 mg) as a yellow oil. To a solution of dihydropyridines (41.4 mg) in $CHCl_3$ (1.0 mL) and MeOH (1 drop) was added MnO_2 (165 mg) at room temperature. After stirring the reaction mixture for 2 h, the reaction mixture was filtered through a pad of Celite and the residue was washed with $CHCl_3$/MeOH (10/1, 30 mL). The filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography (silica gel, $CHCl_3$/MeOH = 60/1) to give **2c** (25.5 mg, 67%, >99% ee) as a pale yellow solid: R_f = 0.40 (silica gel, hexane/AcOEt = 1/3); M.p. 239–241 °C; $[\alpha]_D^{22}$ –173 (*c* 1.03, $CHCl_3$); IR (KBr) 3240 (N–H), 1712 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49-7.45 (m, 5H, Ar*H*), 7.37-7.26 (m, 10H, Ar*H*), 6.34 (brs, 2H, N*H*), 4.88 (dd, *J* = 3.6, 9.9 Hz, 2H, C*H*), 3.75 (dd, *J* = 3.6, 13.7 Hz, 2H, CH_2), 2.76 (dd, *J* = 9.9, 13.7 Hz, 2H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1 (*C*), 167.1 (*C*), 149.5 (*C*), 136.9 (*C*), 130.5 (*C*H), 129.8 (*C*H), 129.6 (*C*), 129.5 (*C*H), 129.2 (*C*H), 127.6 (*C*H), 127.4 (*C*H), 122.8 (*C*), 58.6 (*C*H), 40.1 (*C*H_2). Anal. Calcd for $C_{29}H_{23}N_3O_2$: C, 78.18; H, 5.20; N, 9.43. Found: C, 77.94; H, 5.57; N, 9.12. HRMS (ESI) calcd for $C_{29}H_{24}N_3O_2$ $[M+H]^+$: 446.1869. Found: 446.1862. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H column (hexane/EtOH = 50/50), flow rate 0.5 mL/min, UV detection 254 nm, t_R = 20.4 min.

Characterization for 2d

A solution of **4b**, **5a** and citric acid in MeOH was stirred for 3 h at room temperature and then refluxed

for 12 h. The crude product was purified by column chromatography (silica gel, $CHCl_3$/MeOH = 60/1) to give **2d** (23.5 mg, 33%, >99% ee) as a pale yellow solid: R_f = 0.46 (silica gel, hexane/AcOEt = 1/3); M.p. 289–291 °C; $[\alpha]_D^{26}$ –191 (*c* 0.250, $CHCl_3$); IR (KBr) 3201 (N–H), 2956 (C–H), 1714 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38 (m, 2H, Ar*H*), 7.34-7.22 (m, 13H, Ar*H*), 6.76 (brs, 2H, N*H*), 4.86 (ddd, *J* = 0.9, 3.3, 9.3 Hz, 2H, C*H*), 3.69 (dd, *J* = 3.3, 13.8 Hz, 2H, CH_2), 2.80 (dd, *J* = 9.3, 13.8 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0 (*C*), 167.4 (*C*), 149.7 (*C*), 139.9 (*C*), 136.8 (*C*), 130.7 (*C*H), 129.5 (*C*H), 129.1 (*C*H), 128.2 (*C*H), 127.5 (*C*H), 126.4 (*C*), 122.7 (*C*), 58.5 (*C*H), 40.0 (*C*H_2), 21.7 (*C*H_3). Anal. Calcd for $C_{30}H_{25}N_3O_2$: C, 78.41; H, 5.48; N, 9.14. Found: C, 78.10; H, 5.71; N, 9.40. The enantiomeric excess was determined by HPLC with a Daicel Chiralcel OD-H column (hexane/EtOH = 80/20), flow rate 0.5 mL/min, UV detection 274 nm, t_R = 23.4 min.

Characterization for 2e

A solution of **4c**, **5a** and citric acid in MeOH was stirred for 3 h at room temperature and then refluxed for 17 h. The crude product was purified by column chromatography (silica gel, $CHCl_3$/MeOH = 30/1) to give **2e** (9.8 mg, 43%, >99% ee) as a pale yellow solid: R_f = 0.31 (silica gel, hexane/AcOEt = 1/3); M.p. 279–281 °C; $[\alpha]_D^{25}$ –162 (*c* 1.60, $CHCl_3$); IR (KBr) 3231 (N–H), 2928 (C–H), 1710 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47 (m, 2H, Ar*H*), 7.34-7.24 (m, 10H, Ar*H*), 6.95 (m, 2H, Ar*H*), 6.75 (brs, 2H, N*H*), 4.85 (dd, *J* = 3.3, 9.3 Hz, 2H, C*H*), 3.84 (s, 3H, CH_3), 3.70 (dd, *J* = 3.3, 13.8 Hz, 2H,

CH_2), 2.80 (dd, J = 9.3, 13.8 Hz, 2H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2 (*C*), 167.5 (*C*), 161.1 (*C*), 149.5 (*C*), 136.9 (*C*), 132.8 (*C*H), 129.5 (*C*H), 129.1 (*C*H), 127.5 (*C*H), 122.5 (*C*), 121.3 (*C*), 112.9 (*C*H), 58.5 (*C*H), 55.3 (*C*H_3), 40.0 (*C*H_2). Anal. Calcd for $C_{30}H_{25}N_3O_3$: C, 75.77; H, 5.30; N, 8.84. Found: C, 75.77; H, 5.43; N, 8.89. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H column (hexane/EtOH = 40/60), flow rate 0.5 mL/min, UV detection 274 nm, t_R = 40.0 min.

Characterization for 2f

The crude product was purified by column chromatography (silica gel, $CHCl_3$/MeOH = 70/1) to give **2f** (29.0 mg, 45%, >99% ee) as a pale yellow solid: R_f = 0.46 (silica gel, hexane/AcOEt = 1/3); M.p. 295–300 °C; $[\alpha]_D^{26}$ –44.2 (*c* 0.105, $CHCl_3$); IR (KBr) 3197 (N–H), 3091 (N–H), 2956 (C–H), 2927 (C–H), 1715 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$/CD_3OD (3/1, v/v)) δ 7.53-7.40 (m, 5H, Ar*H*), 4.68 (dd, J = 3.6, 9.6 Hz, 2H, C*H*), 2.05 (ddd, J = 3.6, 9.6, 13.2 Hz, 2H, CH_2), 1.96 (m, 2H, C*H*), 1.53 (ddd, J = 3.6, 9.6, 13.2 Hz, 2H, CH_2), 1.10 (d, J = 6.3 Hz, 6H, CH_3), 1.01 (d, J = 6.3 Hz, 6H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$/CD_3OD (3/1, v/v)) δ 172.4 (*C*), 168.1 (*C*), 148.6 (*C*), 130.0 (*C*H), 129.8 (*C*), 128.9 (*C*H), 126.8 (*C*H), 121.9 (*C*), 55.6 (*C*H), 42.3 (*C*H_2), 25.2 (*C*H), 23.1 (*C*H_3), 21.1 (*C*H_3). Anal. Calcd for $C_{23}H_{27}N_3O_2$: C, 73.18; H, 7.21; N, 11.13. Found: C, 73.19; H, 7.23; N, 11.10. The enantiomeric excess was determined by HPLC with a Daicel Chiralcel OD-H column (hexane/EtOH = 90/10), flow rate 0.5

mL/min, UV detection 274 nm, t_R = 26.9 min.

Characterization for 2g

The crude product was purified by column chromatography (silica gel, $CHCl_3$/MeOH = 60/1) to give **2g** (28.0 mg, 37%, >99% ee) as a pale yellow solid: R_f = 0.46 (silica gel, hexane/AcOEt = 1/3); M.p. 296–298 °C; $[\alpha]_D^{25}$ –133 (*c* 0.825, $CHCl_3$); IR (KBr) 3216 (N–H), 2955 (C–H), 1713 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.73 (brs, 1H, N*H*), 7.52-7.40 (m, 5H, Ar*H*), 7.25-7.15 (m, 6H, Ar*H*, N*H*), 4.82 (dd, *J* = 3.6, 7.8 Hz, 1H, C*H*), 4.66 (dd, *J* = 3.6, 10.2 Hz, 1H, C*H*), 3.60 (dd, *J* = 3.6, 13.8 Hz, 1H, CH_2), 2.86 (dd, *J* = 7.8, 13.8 Hz, 1H, CH_2), 2.08 (ddd, *J* = 3.6, 10.2, 13.4 Hz, 1H, CH_2), 1.90 (m, 1H, C*H*), 1.48 (ddd, *J* = 3.6, 10.2, 13.4 Hz, 1H, CH_2), 1.04 (d, *J* = 6.6 Hz, 3H, CH_3), 1.00 (d, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9 (*C*), 171.0 (*C*), 168.5 (*C*), 167.7 (*C*), 148.9 (*C*), 136.6 (*C*), 130.5 (*C*H), 129.9 (*C*), 129.6 (*C*H), 129.5 (*C*H), 128.9 (*C*H), 127.3 (*C*H), 127.2 (*C*H), 122.6 (*C*), 122.4 (*C*), 58.5 (*C*H), 56.1 (*C*H), 42.8 (*C*H_2), 39.7 (*C*H_2), 25.7 (*C*H), 23.8 (*C*H_3), 21.4 (*C*H_3). Anal. Calcd for $C_{26}H_{25}N_3O_2$: C, 75.89; H, 6.12; N, 10.21. Found: C, 75.82; H, 6.20; N, 10.16. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H column (hexane/EtOH = 70/30), flow rate 0.5 mL/min, UV detection 274 nm, t_R = 18.2 min.

Characterization for 7a

The crude product was purified by column chromatography (silica gel, $CHCl_3$/MeOH = 50/1 to 30/1) to give **7a** (55.4 mg, 93%, >99% ee) as a pale yellow solid: R_f = 0.46 (silica gel, hexane/AcOEt = 1/3); M.p. 163–165 °C; $[\alpha]_D^{26}$ –96.7 (*c* 1.43, $CHCl_3$); IR (KBr) 3216 (N–H), 1698 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46-7.27 (m, 10H, Ar*H*), 6.14 (brs, 1H, N*H*), 4.76 (dd, *J* = 3.3, 10.5 Hz, 1H, C*H*), 3.69 (dd, *J* = 3.3, 13.5 Hz, 1H, CH_2), 2.66 (s, 3H, CH_3), 2.63 (dd, *J* = 10.5, 13.5 Hz, 1H, CH_2), 1.93 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.7 (*C*), 167.5 (*C*), 167.0 (*C*), 158.3 (*C*), 145.6 (*C*), 137.6 (*C*), 137.3 (*C*), 132.8 (*C*), 129.9 (*C*H), 129.8 (*C*H), 129.4 (*C*H), 129.3 (*C*H), 128.5 (*C*H), 127.5 (*C*H), 119.8 (*C*), 58.8 (*C*H), 40.2 (*C*H_2), 32.0 (*C*H_3), 23.5 (*C*H_3). Anal. Calcd for $C_{23}H_{20}N_2O_2$: C, 77.51; H, 5.66; N, 7.86. Found: C, 77.13; H, 5.68; N, 7.50. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IC column (hexane/EtOH = 80/20), flow rate 0.5 mL/min, UV detection 274 nm, t_R = 26.7 min.

Characterization for 7b

The crude product was purified by column chromatography (silica gel, $CHCl_3$/MeOH = 60/1) to give **7b** (39.6 mgl, 89%, >99% ee) as a pale yellow oil: R_f = 0.54 (silica gel, hexane/AcOEt = 1/3); $[\alpha]_D^{25}$ –104 (*c* 1.16, $CHCl_3$); IR (KBr) 3414 (N–H), 3245 (N–H), 1732 (C=O), 1703 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44-7.25 (m, 10H, Ar*H*), 6.22 (brs, 1H, N*H*), 4.75 (dd, *J* = 3.3, 10.2 Hz, 1H, C*H*),

3.67 (dd, J = 3.3, 13.8 Hz, 1H, CH_2), 3.58 (s, 3H, CH_3), 2.73 (s, 3H, CH_3), 2.64 (dd, J = 10.2, 13.8 Hz, 1H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8 (*C*), 167.5 (*C*), 167.3 (*C*), 159.7 (*C*), 147.3 (*C*), 137.3 (*C*), 133.3 (*C*), 130.2 (*C*), 129.4 (*C*H), 129.3 (*C*H), 129.2 (*C*H), 129.0 (*C*H), 128.1 (*C*H), 127.5 (*C*H), 120.0 (*C*), 58.8 (*C*H), 52.6 (*C*H_3), 40.2 (*C*H_2), 23.5 (*C*H_3). Anal. Calcd for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52. Found: C, 74.06; H, 5.37; N, 7.46. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IC column (hexane/EtOH = 70/30), flow rate 0.5 mL/min, UV detection 274 nm, t_R = 19.9 min.

Characterization for 7c

The crude product was purified by column chromatography (silica gel, hexane/AcOEt = 1/2 to 1/4) to give **7c** (66.0 mg, 78%, >99% ee) as a pale yellow solid: R_f = 0.37 (silica gel, hexane/AcOEt = 1/3); M.p. 135–137 °C; $[\alpha]_D^{28}$ –92.1 (*c* 1.72, $CHCl_3$); IR (KBr) 3407 (N–H), 3255 (N–H), 2921 (C–H), 1700 (C=O), 1658 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47-7.07 (m, 15H, Ar*H*), 6.27 (brs, 1H, N*H*), 4.74 (dd, J = 3.3, 10.2 Hz, 1H, C*H*), 3.67 (dd, J = 3.3, 13.8 Hz, 1H, CH_2), 2.83 (s, 3H, CH_3), 2.61 (dd, J = 10.2, 13.8 Hz, 1H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7 (*C*), 167.4 (*C*), 166.0 (*C*), 160.6 (*C*), 146.3 (*C*), 137.13 (*C*), 137.06 (*C*), 132.8 (*C*), 132.6 (*C*), 129.5 (*C*H), 129.4 (*C*H), 129.3 (*C*H), 129.1 (*C*H), 128.3 (*C*H), 127.4 (*C*H), 125.4 (*C*H), 121.0 (*C*H), 119.8 (*C*), 58.8 (*C*H), 39.9 (*C*H_2), 23.5 (*C*H_3). Anal. Calcd for $C_{28}H_{23}N_3O_2$: C, 77.58; H, 5.35; N, 9.69. Found: C, 77.55; H, 5.47; N, 9.74. The

enantiomeric excess was determined by HPLC with a Daicel Chiralpak IE column (hexane/EtOH = 60/40), flow rate 0.5 mL/min, UV detection 274 nm, t_R = 16.7 min.

Characterization for 7d

The crude product was purified by column chromatography (silica gel, $CHCl_3$/MeOH = 60/1 to 30/1) to give **7d** (62.0 mg, 87%, >99% ee) as a pale yellow oil: R_f = 0.60 (silica gel, hexane/AcOEt = 1/3); $[\alpha]_D^{26}$ –63.3 (*c* 1.05, $CHCl_3$); IR (KBr) 3403 (N–H), 3259 (N–H), 1701 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.60 (ddd, *J* = 0.9, 1.8, 4.5 Hz, 1H, Ar*H*), 8.38 (dt, *J* = 0.9, 8.1 Hz, 1H, Ar*H*), 7.88 (dt, *J* = 1.8, 8.1 Hz, 1H, Ar*H*), 7.44-7.23 (m, 11H, Ar*H*), 6.61 (brs, 1H, N*H*), 4.85 (ddd, *J* = 0.9, 3.9, 9.6 Hz, 1H, C*H*), 4.04 (q, *J* = 7.2 Hz, 2H, CH_2), 3.66 (dd, *J* = 3.9, 13.8 Hz, 1H, CH_2), 2.77 (dd, *J* = 9.6, 13.8 Hz, 1H, CH_2), 0.98 (t, *J* = 7.2 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0 (*C*), 167.2 (*C*), 166.8 (*C*), 156.7 (*C*), 155.4 (*C*), 148.7 (*C*H), 148.6 (*C*), 137.2 (*C*H), 137.1 (*C*), 133.0 (*C*), 130.0 (*C*), 129.5 (*C*H), 129.1 (*C*H), 127.9 (*C*H), 127.4 (*C*H), 124.6 (*C*H), 123.7 (*C*H), 122.0 (*C*), 61.4 (*C*H_2), 58.8 (*C*H), 40.0 (*C*H_2), 13.7 (*C*H_3). Anal. Calcd for $C_{28}H_{23}N_3O_3$: C, 74.82; H, 5.16; N, 9.35. Found: C, 74.77; H, 5.29; N, 9.28. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak AD-H column (hexane/EtOH = 60/40), flow rate 0.5 mL/min, UV detection 274 nm, t_R = 19.5 min.

References

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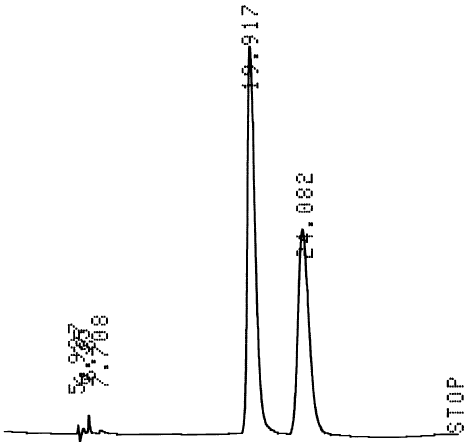
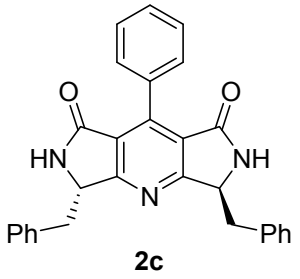
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK® AD-H (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 50/50; Flow rate: 0.5 mL/min; UV detection: 254 nm.

D,L mixture of **2c**

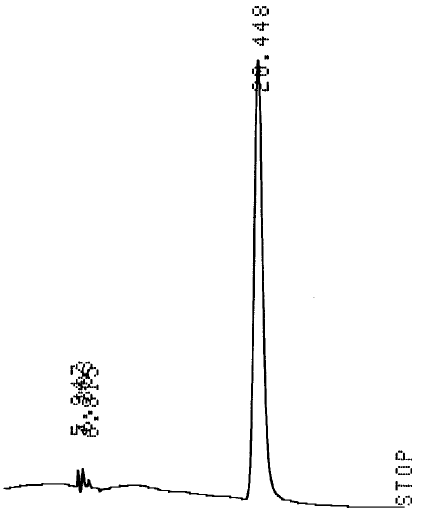




2c

TIME	AREA	MK	IDNO	CONC
5.937	930			0.3213
6.35	1980			0.6839
6.8	2147	V		0.7418
7.708	441			0.1523
19.917	160903			55.5883
24.082	123054			42.5123
TOTAL	289454			100

Enantiomerically enriched (–)–**2c** (>99% ee)

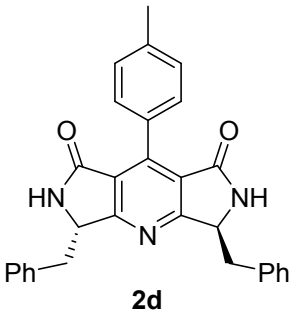


TIME	AREA	MK	IDNO	CONC
5.947	1585			0.755
6.333	2960			1.4101
6.815	1119	V		0.5331
20.448	204276			97.3018
TOTAL	209940			100

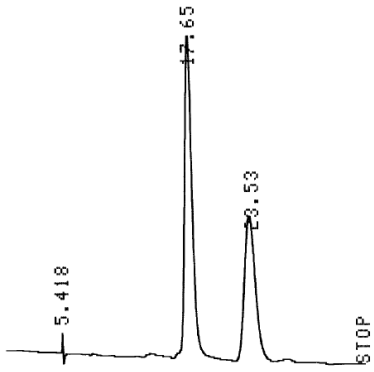
HPLC Chromatographic Conditions

Column: Daicel CHIRALCEL® OD-H (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 80/20; Flow rate: 0.5 mL/min; UV detection: 274 nm.

D,L mixture of **2d**

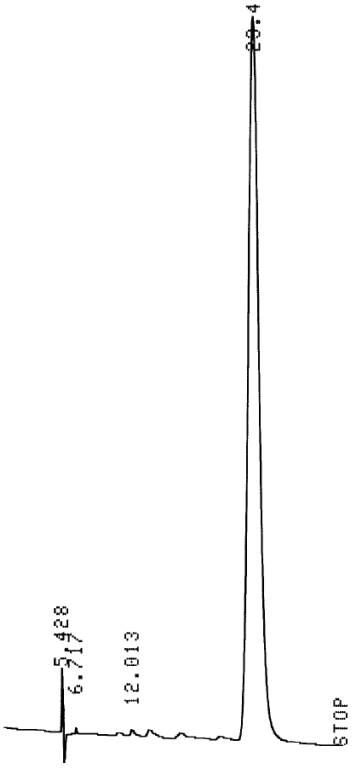


2d



TIME	AREA	MK	IDNO	CONC
5.418	1689			0.5665
17.65	176162			59.098
23.53	120233			40.3355
	---------			----------
TOTAL	298084			100

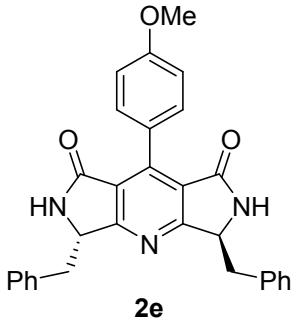
Enantiomerically enriched (–)–**2d** (>99% ee)



TIME	AREA	MK	IDNO	CONC
5.428	8420			1.4618
6.717	553			0.096
12.013	920			0.1598
23.4	566140			98.2825
	---------			----------
TOTAL	576033			100

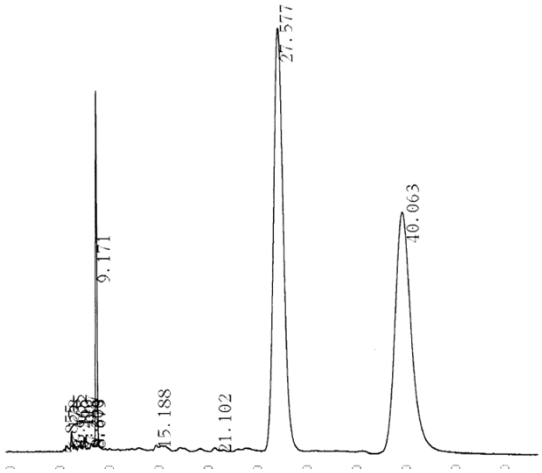
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK® AD-H (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 40/60; Flow rate: 0.5 mL/min; UV detection: 274 nm.



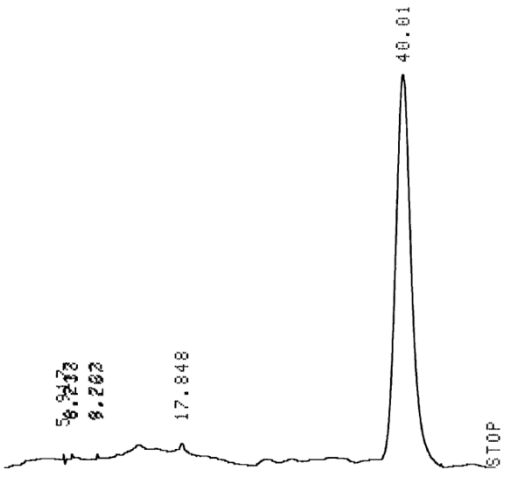
2e

D,L mixture of **2e**



TIME	AREA	HEIGHT	MK	IDNO	CONC
5.855	174	28			0.0249
6.178	1166	70	V		0.1667
6.655	2576	228	V		0.3684
6.965	757	77	V		0.1083
7.44	1051	61	V		0.1504
7.927	1818	146	V		0.26
8.3	375	31	V		0.0536
8.673	1199	73	V		0.1715
9.171	42147	4100	V		6.0284
15.188	679	40			0.0972
21.102	887	38			0.1269
27.577	328756	4850			47.0221
40.063	317565	2763			45.4215
TOTAL	699151	12506			100

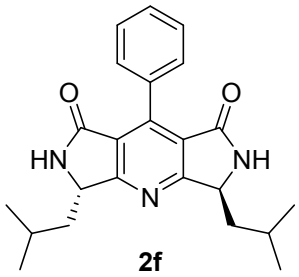
Enantiomerically enriched (–)–**2e** (>99% ee)



TIME	AREA	MK	IDNO	CONC
5.917	579			0.1162
6.217	846			0.1698
6.733	957	V		0.192
8.733	234			0.0469
9.267	877			0.176
17.848	2011			0.4034
40.01	493014			98.8958
TOTAL	498518			100

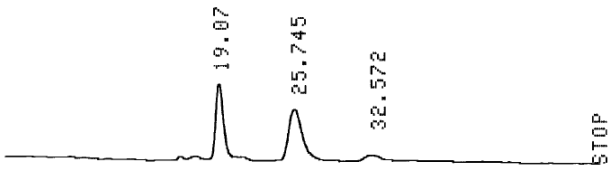
HPLC Chromatographic Conditions

Column: Daicel CHIRALCEL® OD-H (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 90/10; Flow rate: 0.5 mL/min; UV detection: 274 nm.



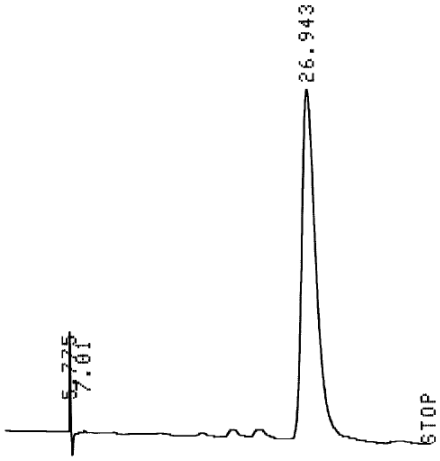
2f

D,L mixture of **2f**



TIME	AREA	MK	IDNO	CONC
19.07	34990			42.3937
25.745	43366			52.5414
32.572	4180			5.0649
TOTAL	82537			100

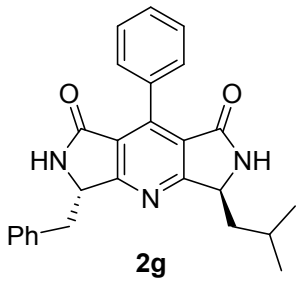
Enantiomerically enriched (–)–**2f** (>99% ee)



TIME	AREA	MK	IDNO	CONC
5.775	6662			2.0808
7.01	275			0.0858
26.943	313223			97.8334
TOTAL	320159			100

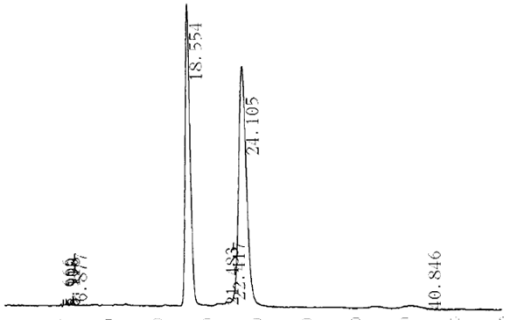
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK® AD-H (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 70/30; Flow rate: 0.5 mL/min; UV detection: 274 nm.



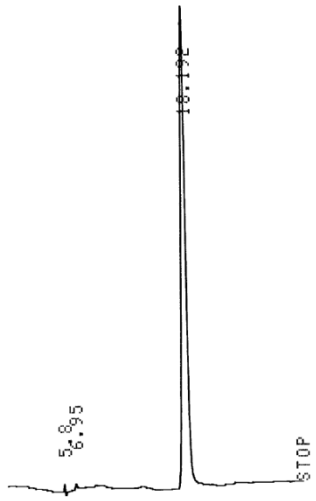
2g

D,L mixture of **2g**



TIME	AREA	HEIGHT	MK	IDNO	CONC
5.666	181	30			0.0646
5.9	134	12			0.0477
6.118	220	21	V		0.0784
6.877	882	110			0.3152
18.554	119482	3458			42.6906
21.483	1387	25			0.4956
22.417	1735	45	V		0.6198
24.105	152634	2756	V		54.5354
40.846	3226	32			1.1526
TOTAL	279880	6489			100

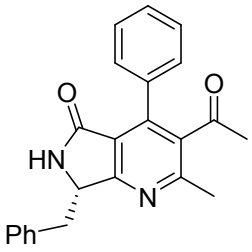
Enantiomerically enriched (–)–**2g** (>99% ee)



TIME	AREA	MK	IDNO	CONC
5.8	856			0.4503
6.95	615			0.3236
18.192	188564			99.2261
TOTAL	190035			100

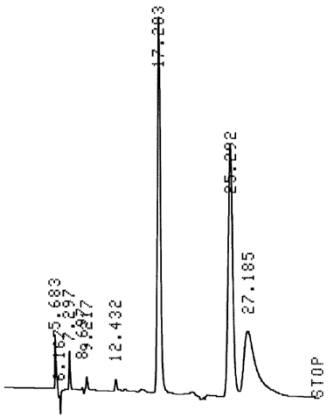
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK® IC (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 80/20; Flow rate: 0.5 mL/min; UV detection: 274 nm.



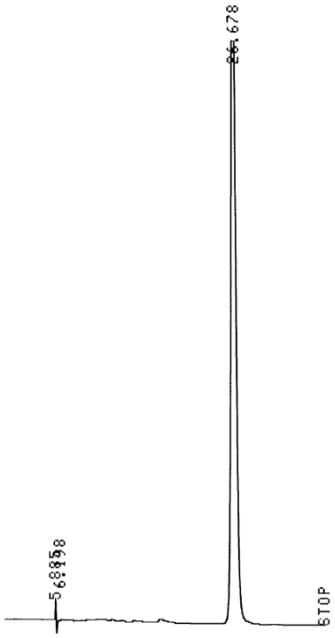
7a

Racemic standard of **7a**



TIME	AREA	MK	IDNO	CONC
5.683	7910			2.3946
6.167	1067			0.3231
7.297	4925			1.4911
8.697	515			0.1558
9.217	3003			0.909
12.432	2222			0.6728
17.283	118334			35.8232
25.292	118166			35.7726
27.185	74184	V		22.4579
TOTAL	330326			100

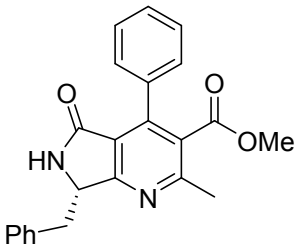
Enantiomerically enriched (–)–**7a** (>99% ee)



TIME	AREA	MK	IDNO	CONC
5.885	2827			0.7431
6.198	1798			0.4725
26.678	375830			98.7843
TOTAL	380455			100

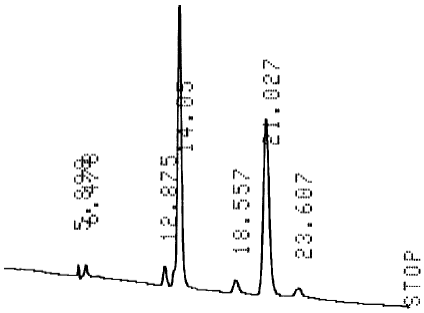
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAC® IC (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 70/30; Flow rate: 0.5 mL/min; UV detection: 274 nm.



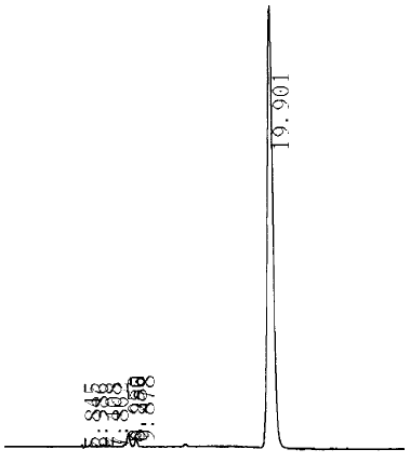
7b

Racemic standard of **7b**



TIME	AREA	MK	IDNO	CONC
5.898	822			0.6687
6.478	1276			1.0382
12.875	3482			2.8333
14.05	57436			46.7299
18.557	3595			2.9247
21.027	53484			43.5144
23.607	2816			2.2908
TOTAL	122912			100

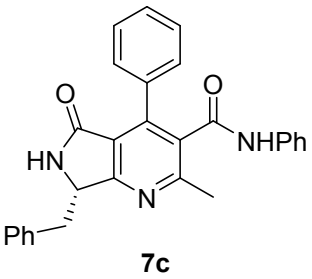
Enantiomerically enriched (–)–**7b** (>99% ee)



TIME	AREA	HEIGHT	MK	IDNO	CONC
5.845	171	27			0.1513
6.386	140	16			0.1241
7.408	243	24			0.2152
7.862	260	19	V		0.2301
8.95	222	14			0.1971
9.285	1686	115	V		1.4949
9.878	1128	78	V		1.0001
19.901	108917	3746			96.5872
TOTAL	112766	4039			100

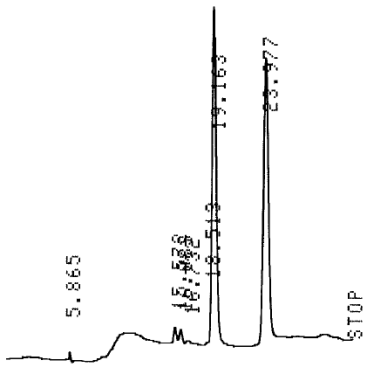
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK® IE (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 60/40; Flow rate: 0.5 mL/min; UV detection: 274 nm.



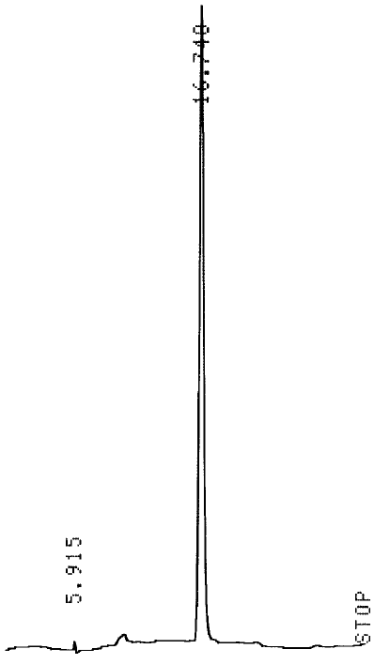
7c

Racemic standard of **7c**



TIME	AREA	MK	IDNO	CONC
5.865	862			0.4347
15.572	3340			1.6836
16.083	3001	V		1.5126
16.732	924			0.466
18.513	613			0.3088
19.163	94063	V		47.4173
23.977	95570			48.177
TOTAL	198373			100

Enantiomerically enriched (–)–**7c** (>99% ee)

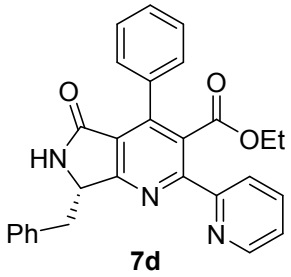


TIME	AREA	MK	IDNO	CONC
5.915	930			0.5596
16.748	165243			99.4404
TOTAL	166173			100

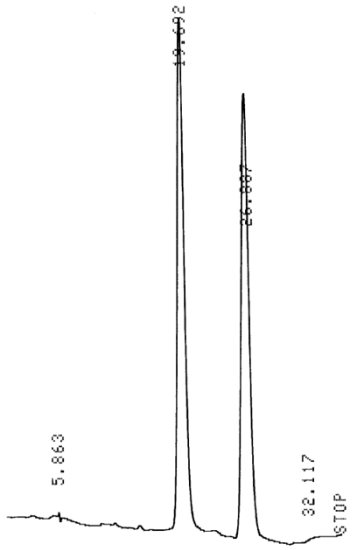
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK® AD-H (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 60/40; Flow rate: 0.5 mL/min; UV detection: 274 nm.

Racemic standard of **7d**

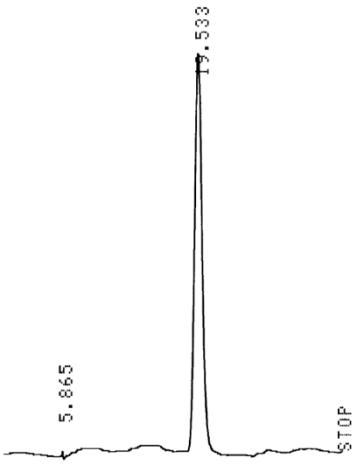


7d

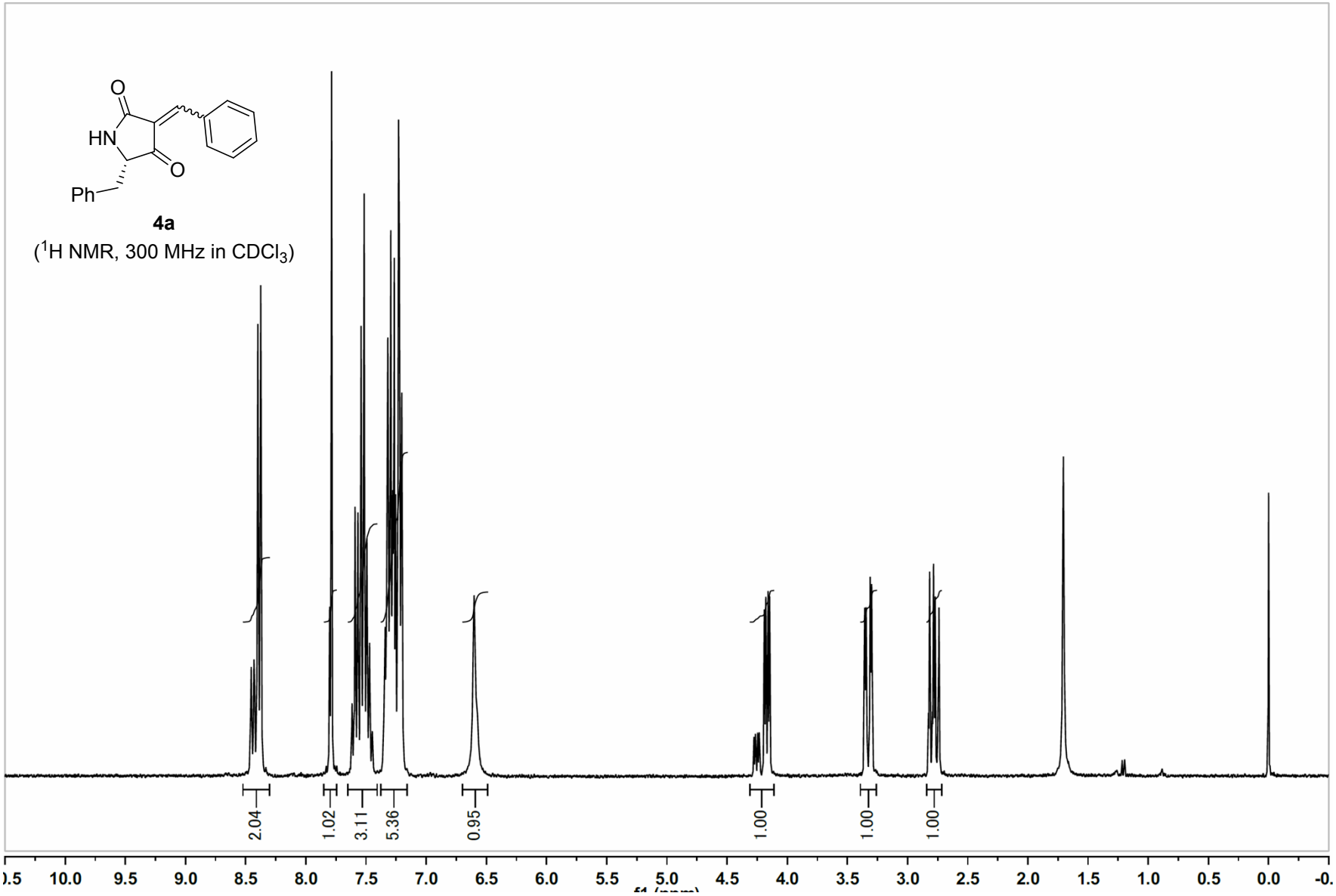


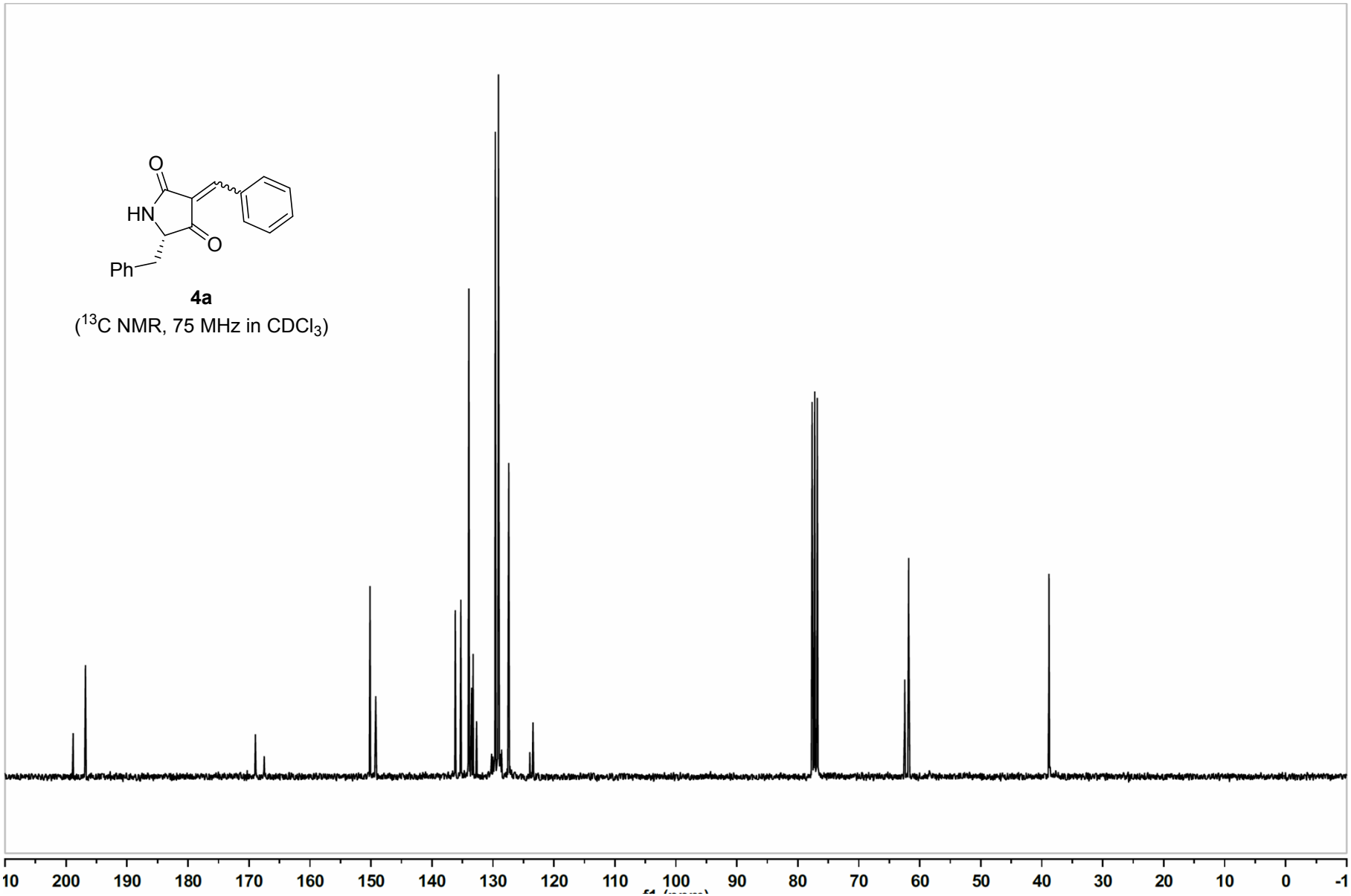
TIME	AREA	MK	IDNO	CONC
5.863	670			0.0945
19.692	357898			50.4522
26.887	350496			49.4088
32.117	316			0.0445
TOTAL	709380			100

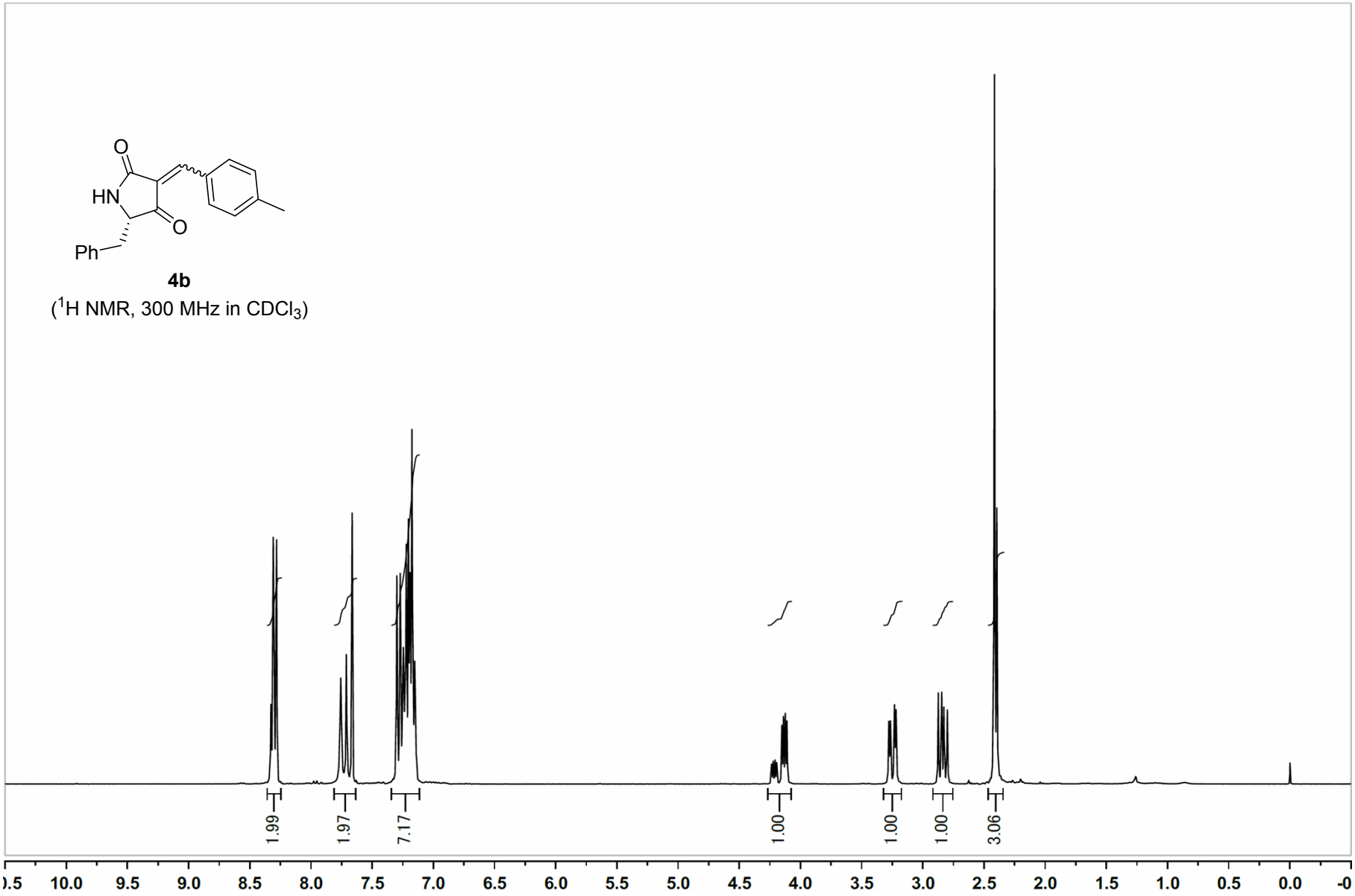
Enantiomerically enriched (–)–**7d** (>99% ee)

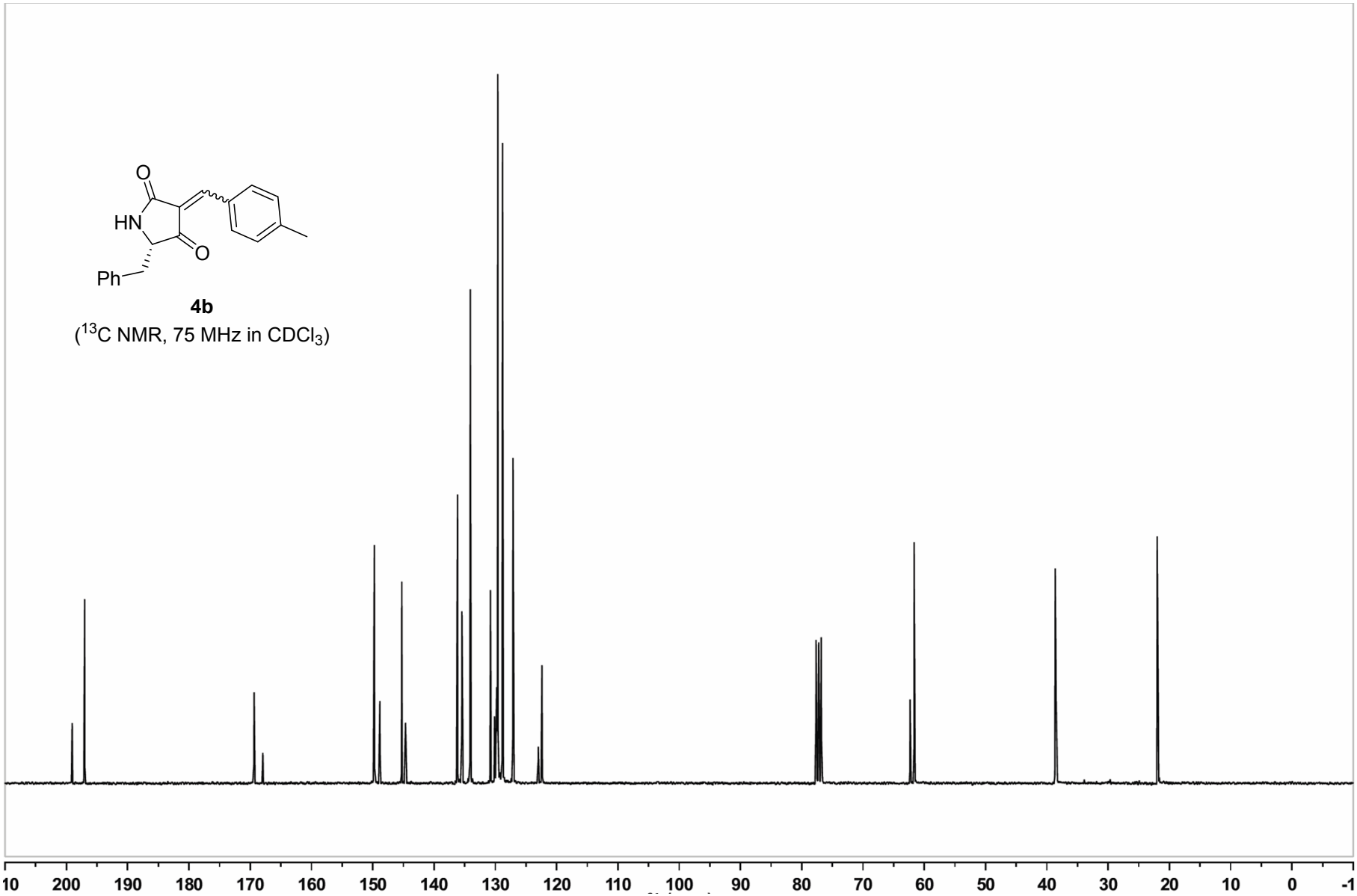


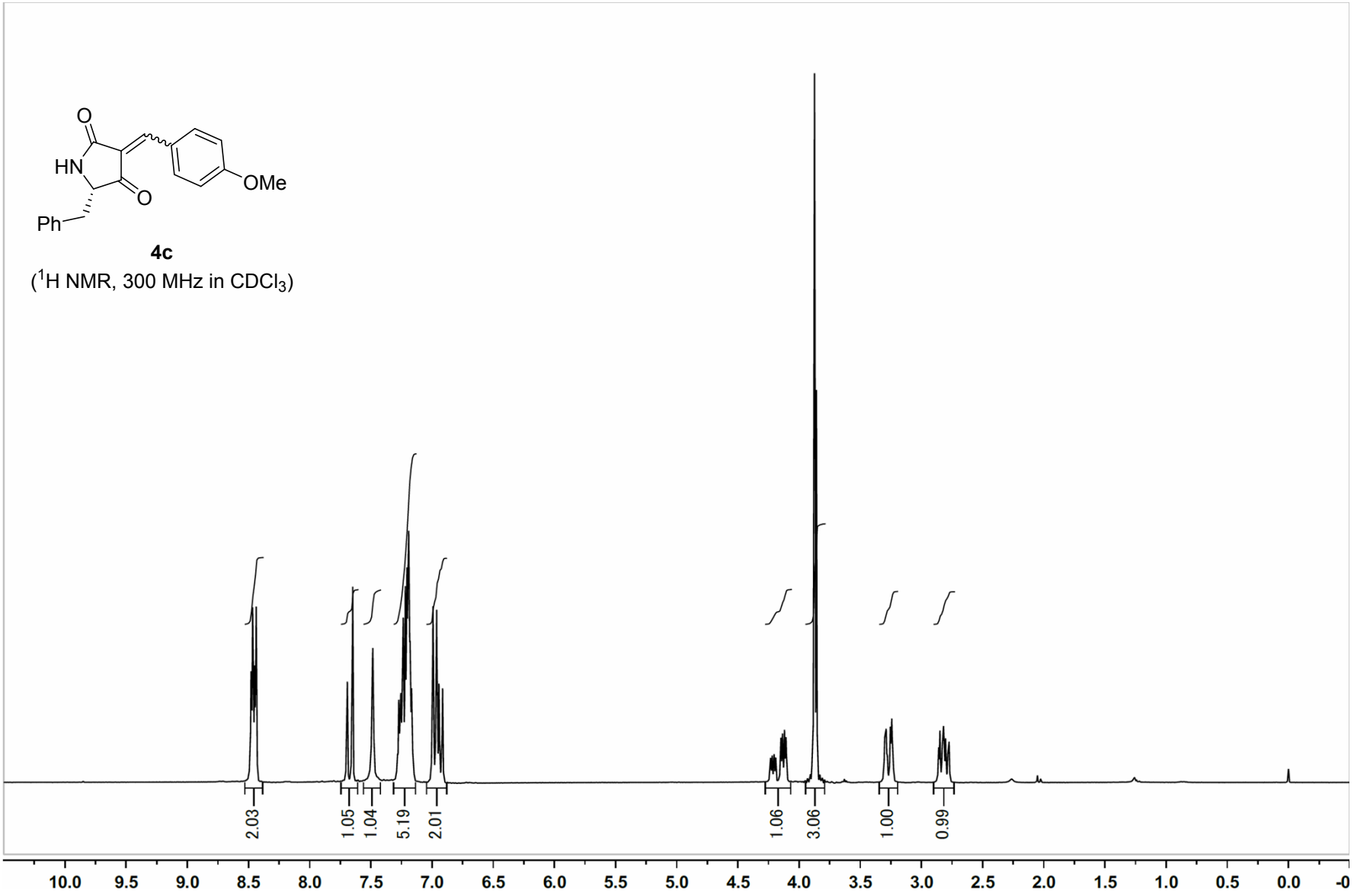
TIME	AREA	MK	IDNO	CONC
5.865	535			0.2205
19.533	242178			99.7794
TOTAL	242713			100


O
HN
O
Ph
4a
(1H NMR, 300 MHz in CDCl3)
2.04
1.02
3.11
5.36
0.95
1.00
1.00
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


O
HN
O
Ph
4a
(^{13}C NMR, 75 MHz in $CDCl_3$)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1

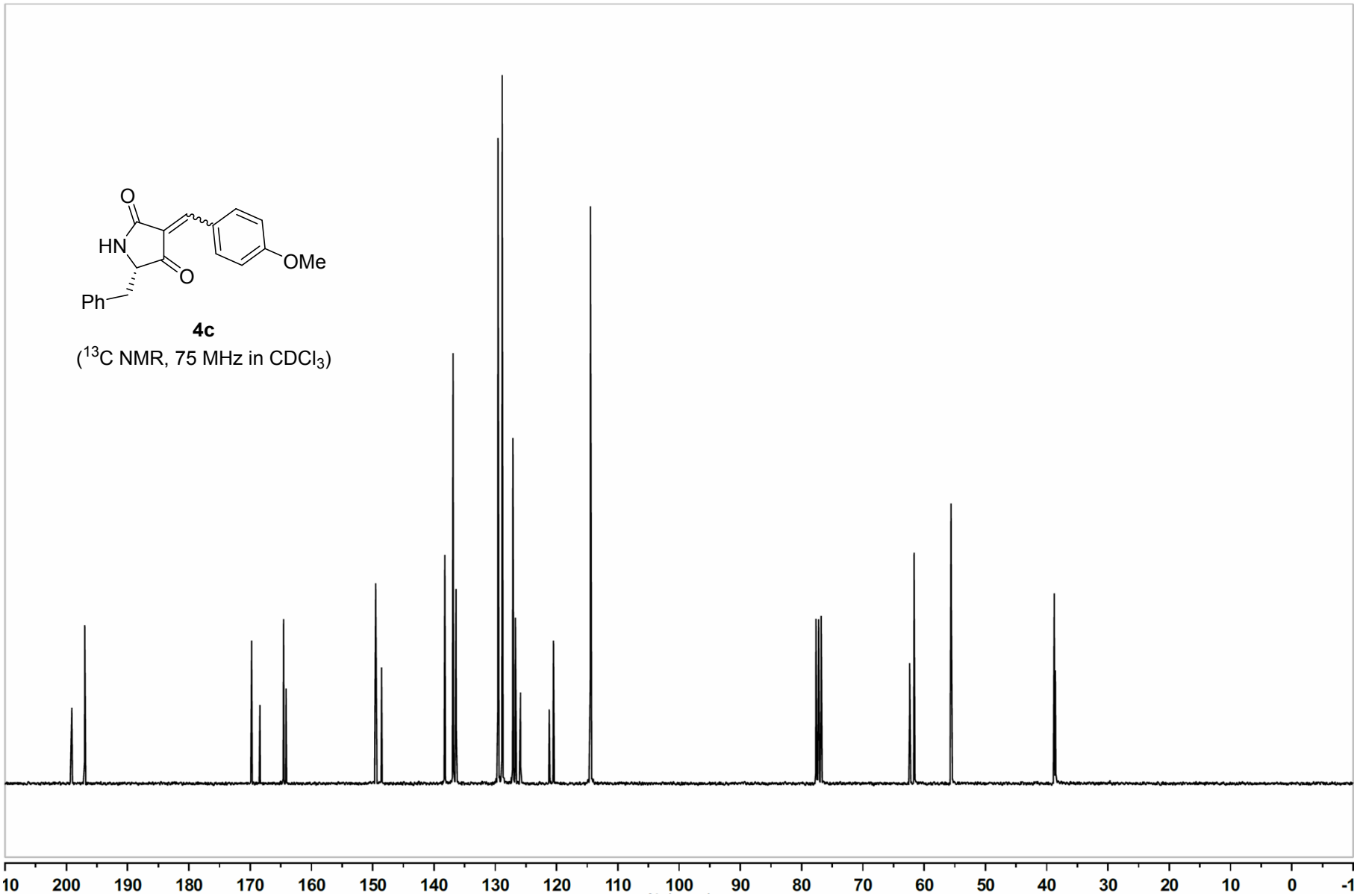

O
HN
O
Ph
4b
(1H NMR, 300 MHz in CDCl3)
1.99
1.97
7.17
1.00
1.00
1.00
3.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

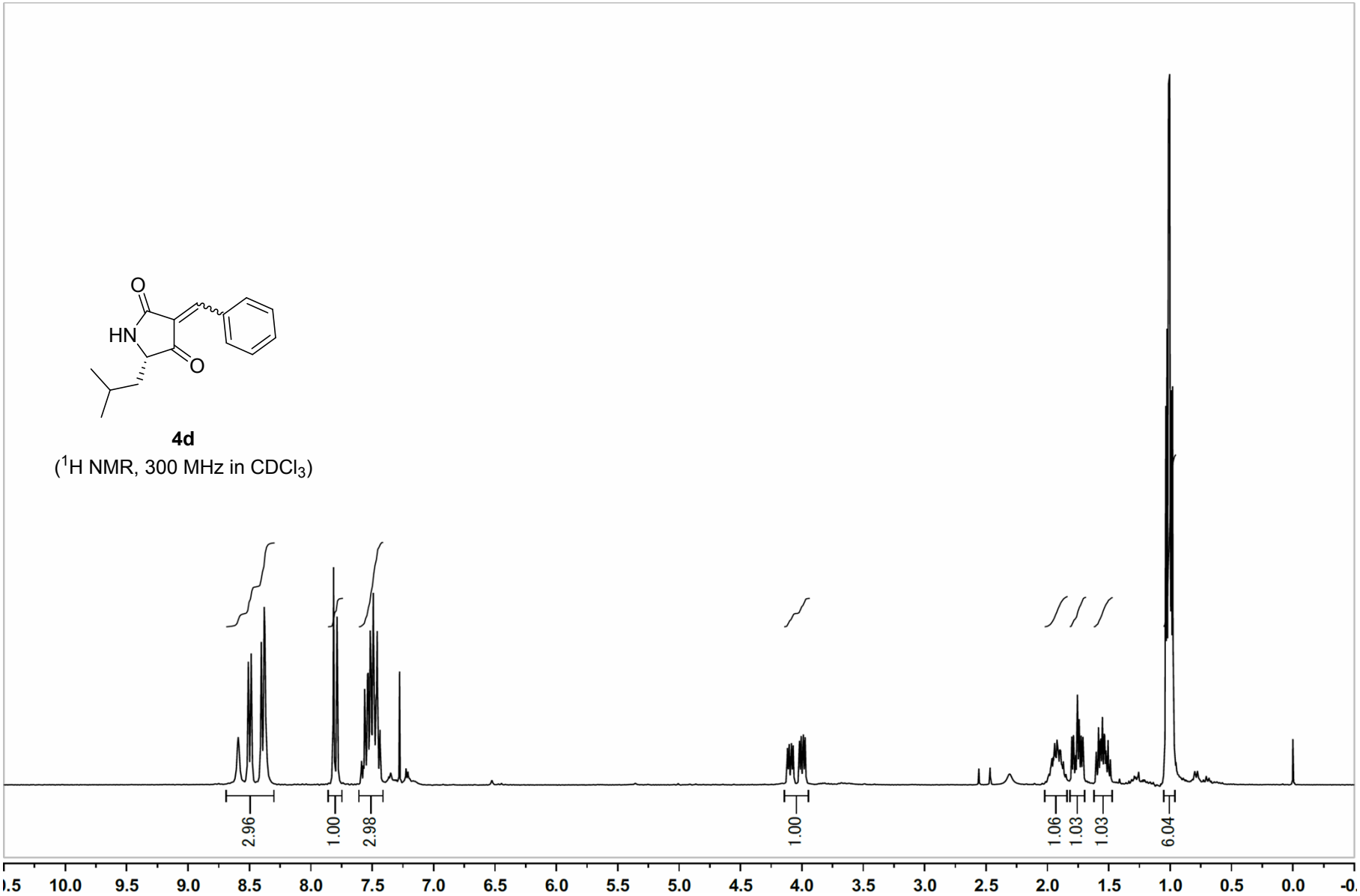

O
HN
O
Ph
4b
(13C NMR, 75 MHz in CDCl3)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1

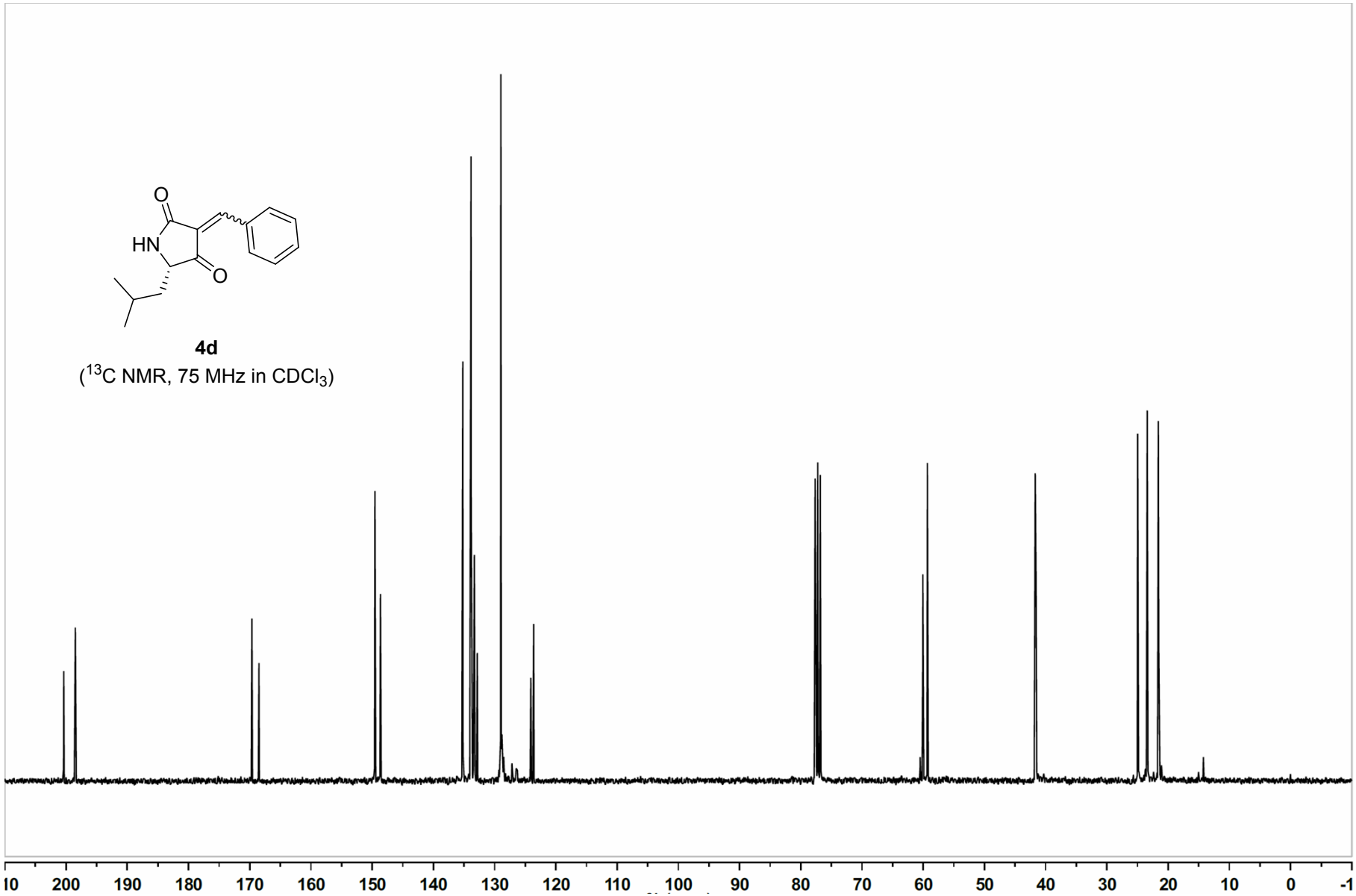


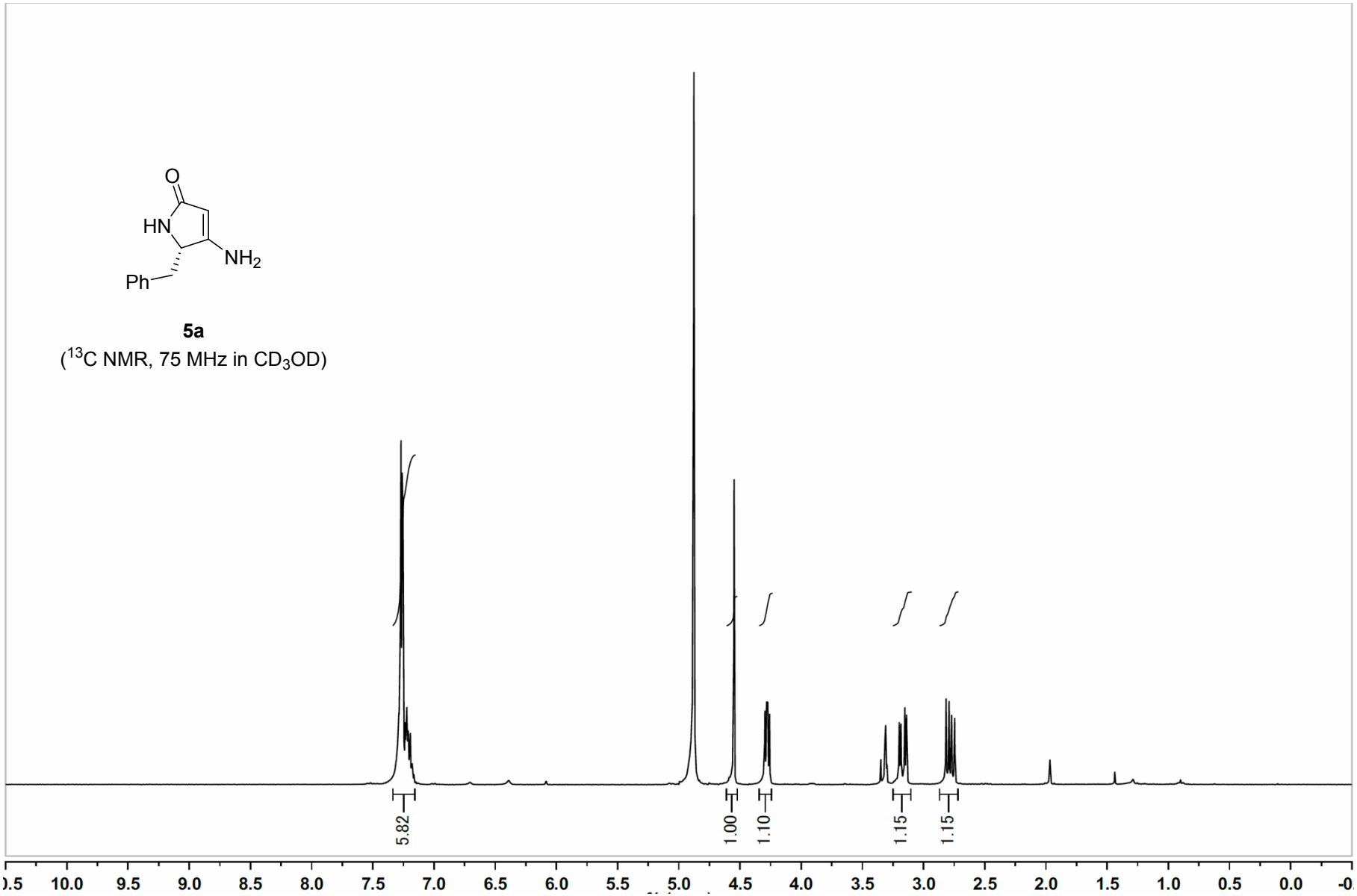
4c

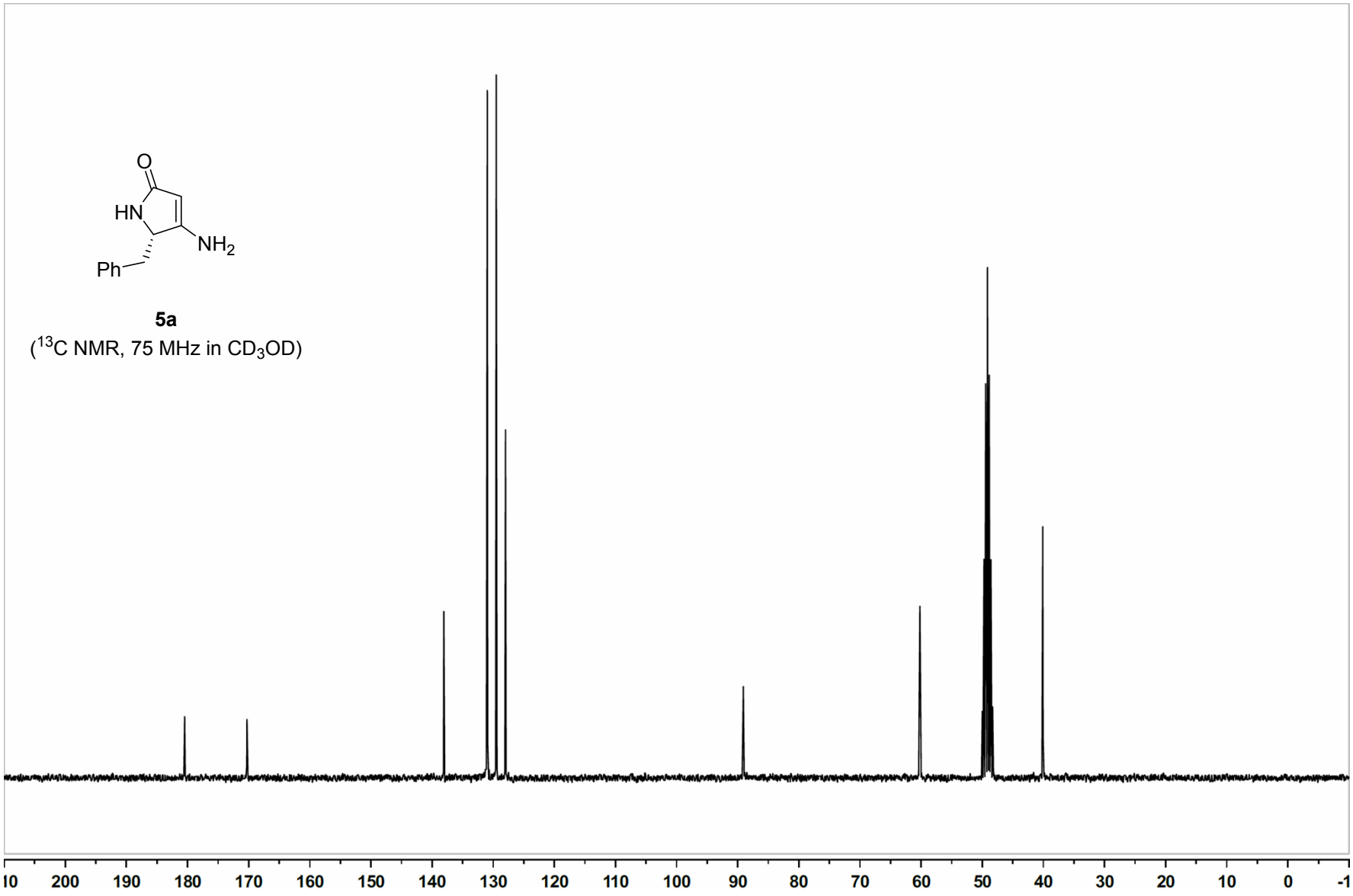
(^{1}H NMR, 300 MHz in $CDCl_3$)

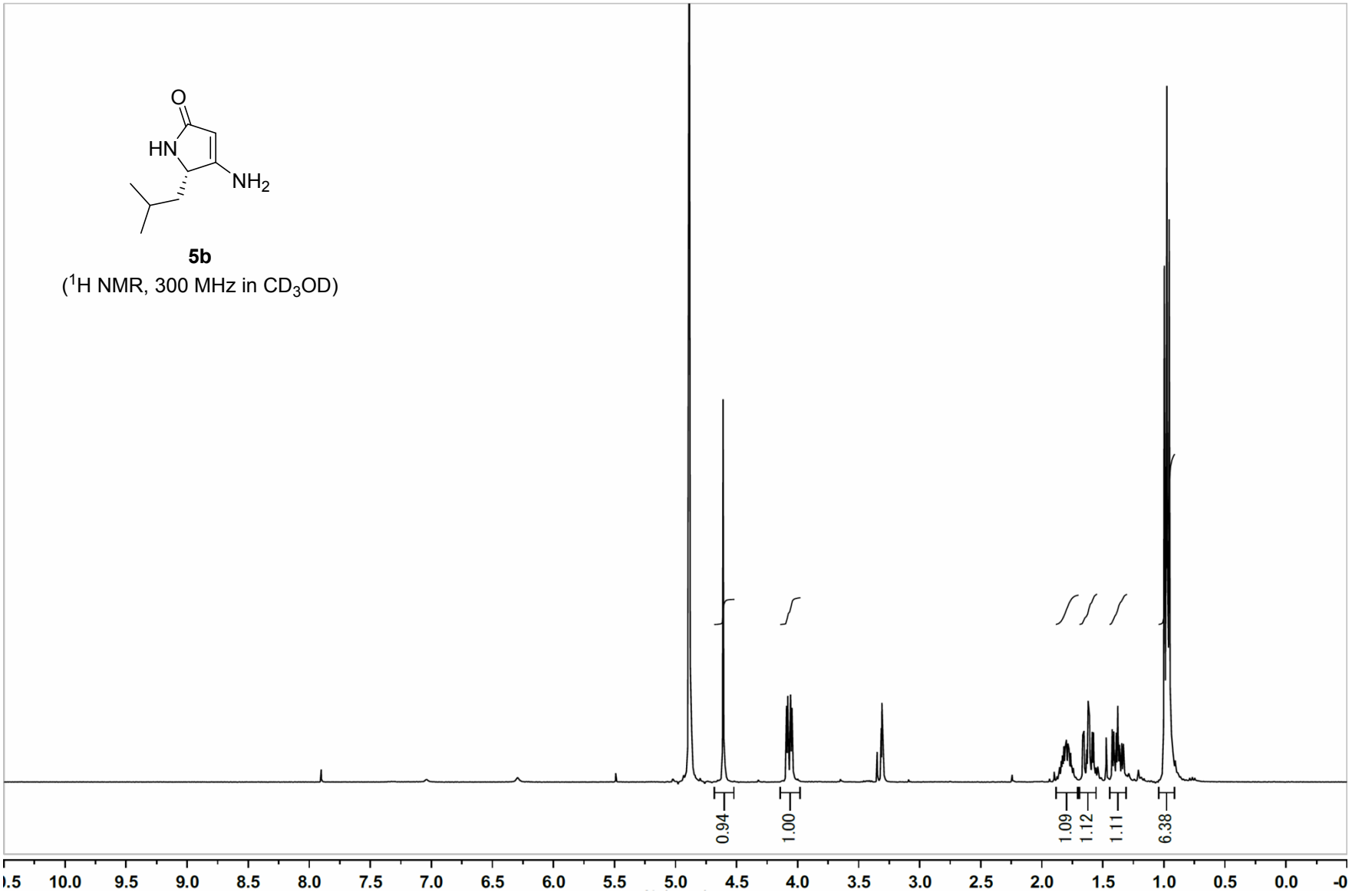

O
HN
O
OMe
Ph
4c
(^{13}C NMR, 75 MHz in $CDCl_3$)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1


O
HN
O
4d
(1H NMR, 300 MHz in CDCl3)
2.96
1.00
2.98
1.00
1.06
1.03
1.03
6.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


O
HN
O
4d
(13C NMR, 75 MHz in CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

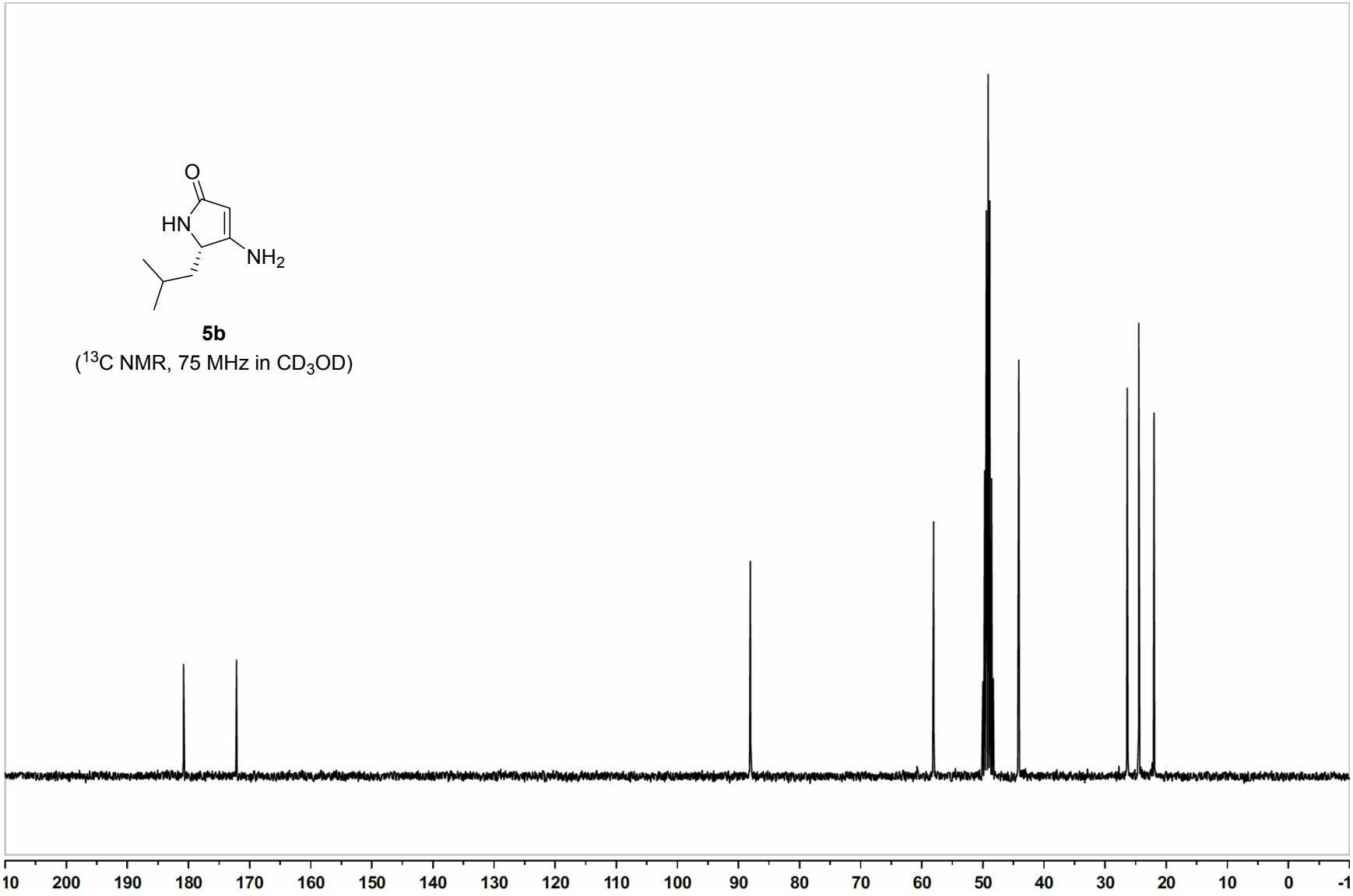

O
HN
NH2
Ph
5a
(13C NMR, 75 MHz in CD3OD)
5.82
1.00
1.10
1.15
1.15
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

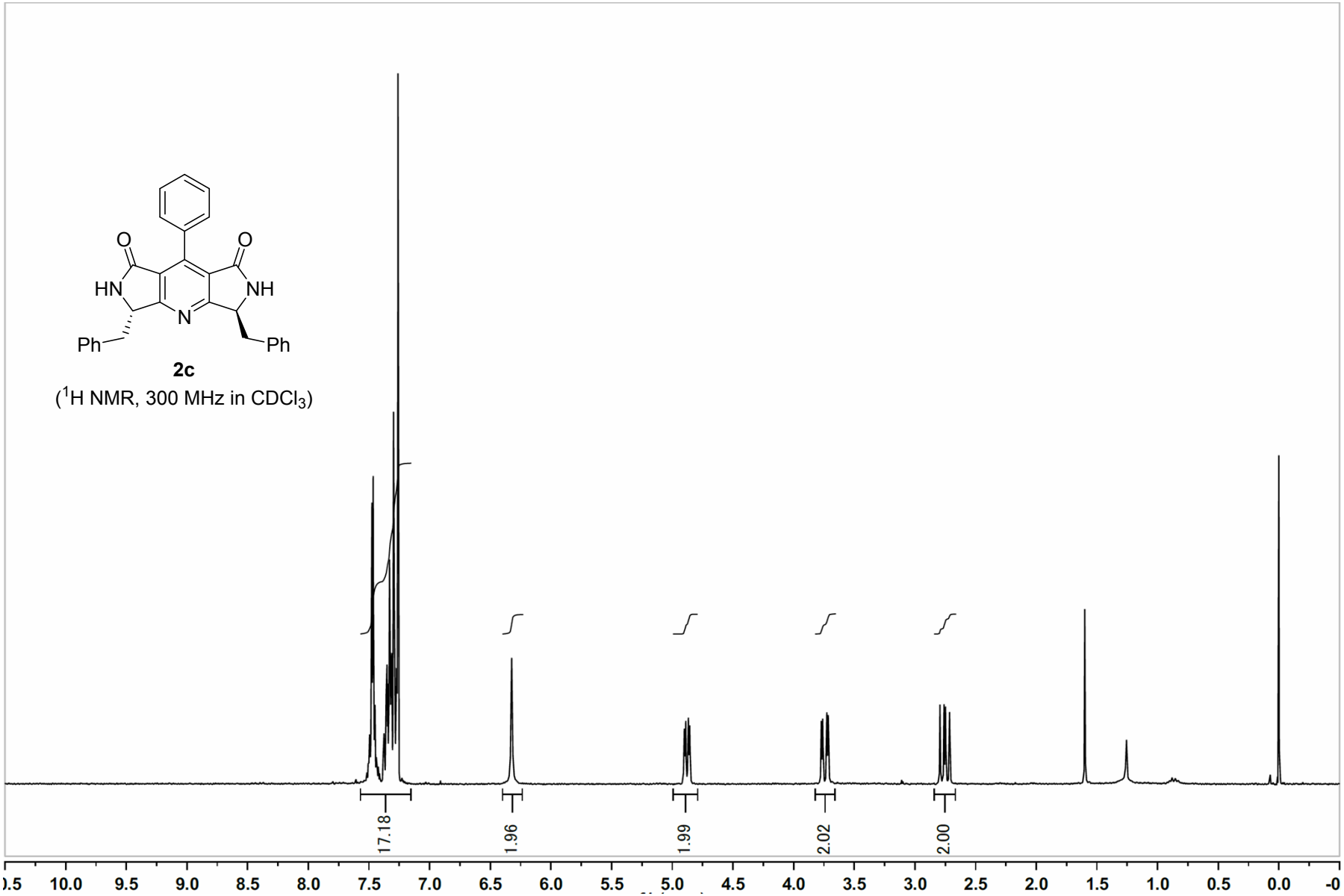

O
HN
NH2
Ph
5a
(13C NMR, 75 MHz in CD3OD)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

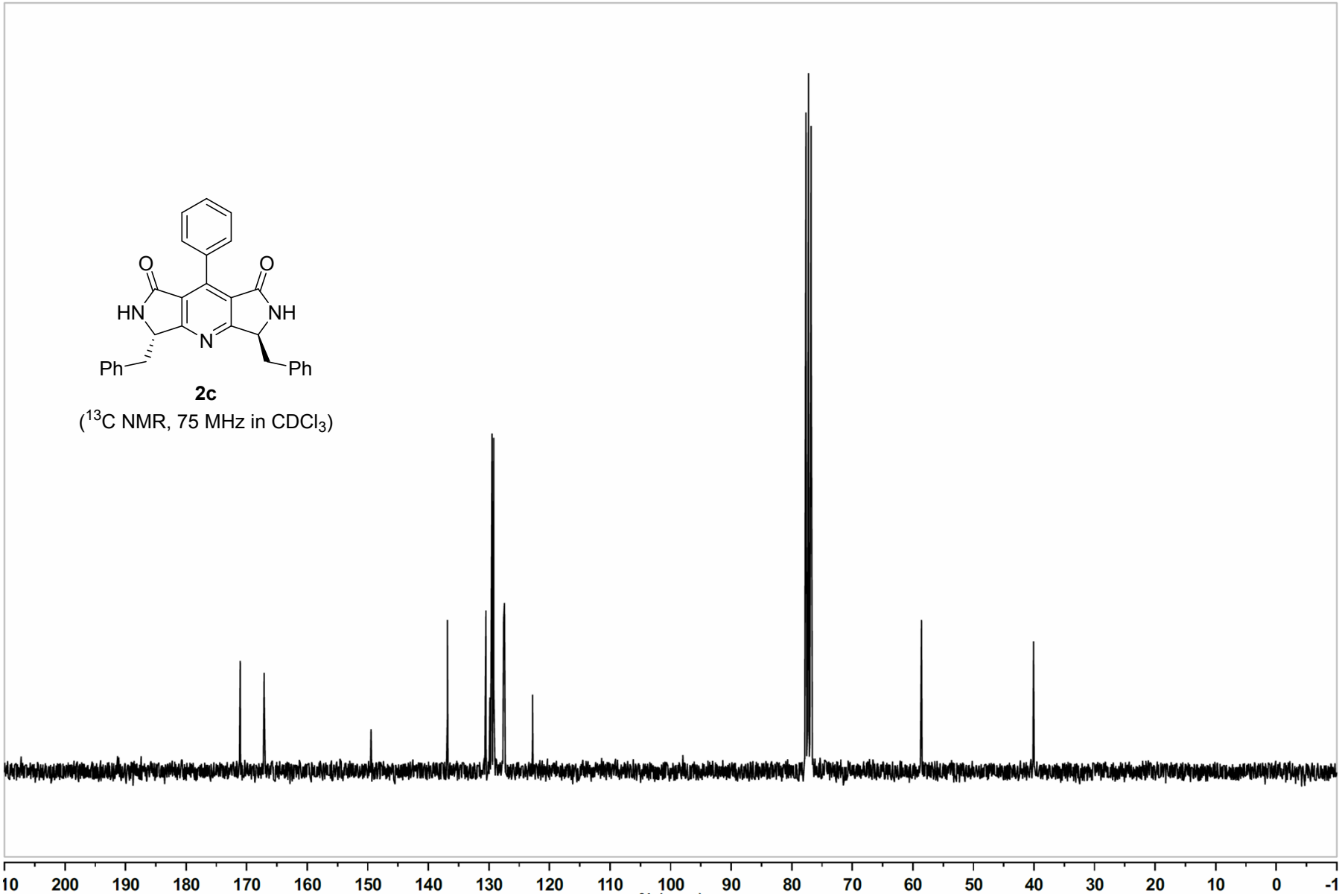


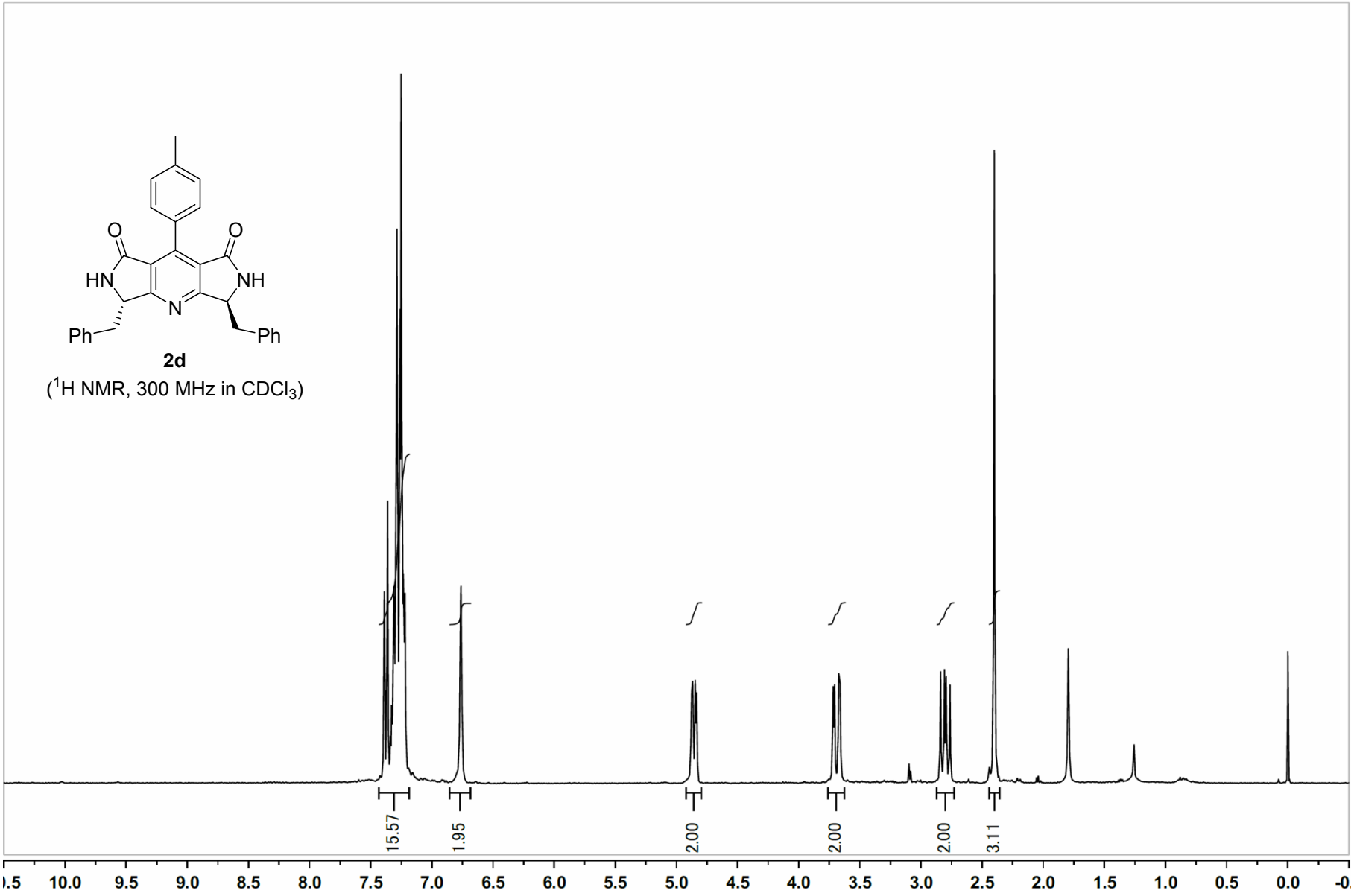
5b

(^{1}H NMR, 300 MHz in CD_3OD)


O
HN
NH2
5b
(13C NMR, 75 MHz in CD3OD)
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1

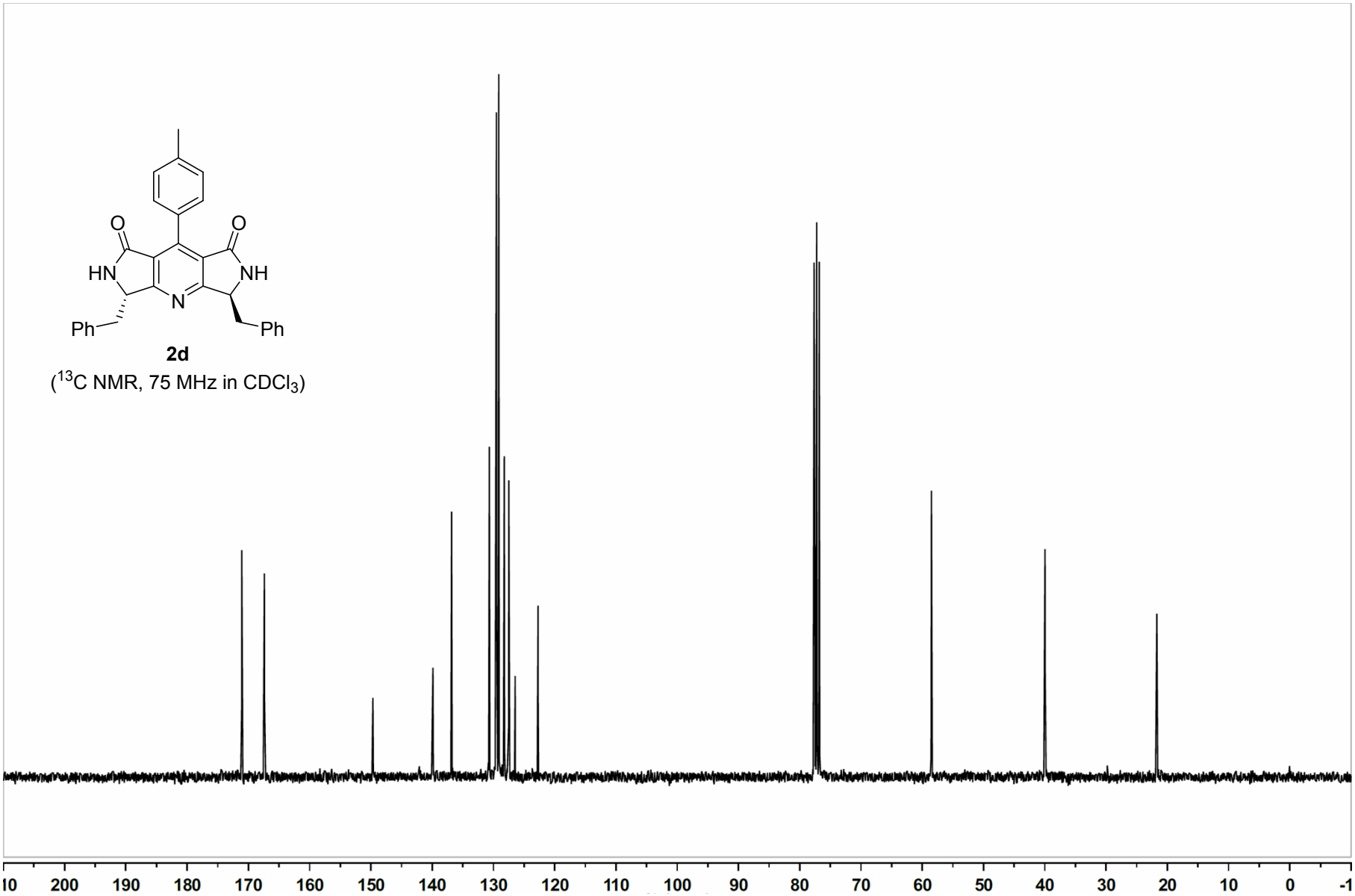

O
O
HN
NH
N
Ph
Ph
2c
(1H NMR, 300 MHz in CDCl3)
17.18
1.96
1.99
2.02
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

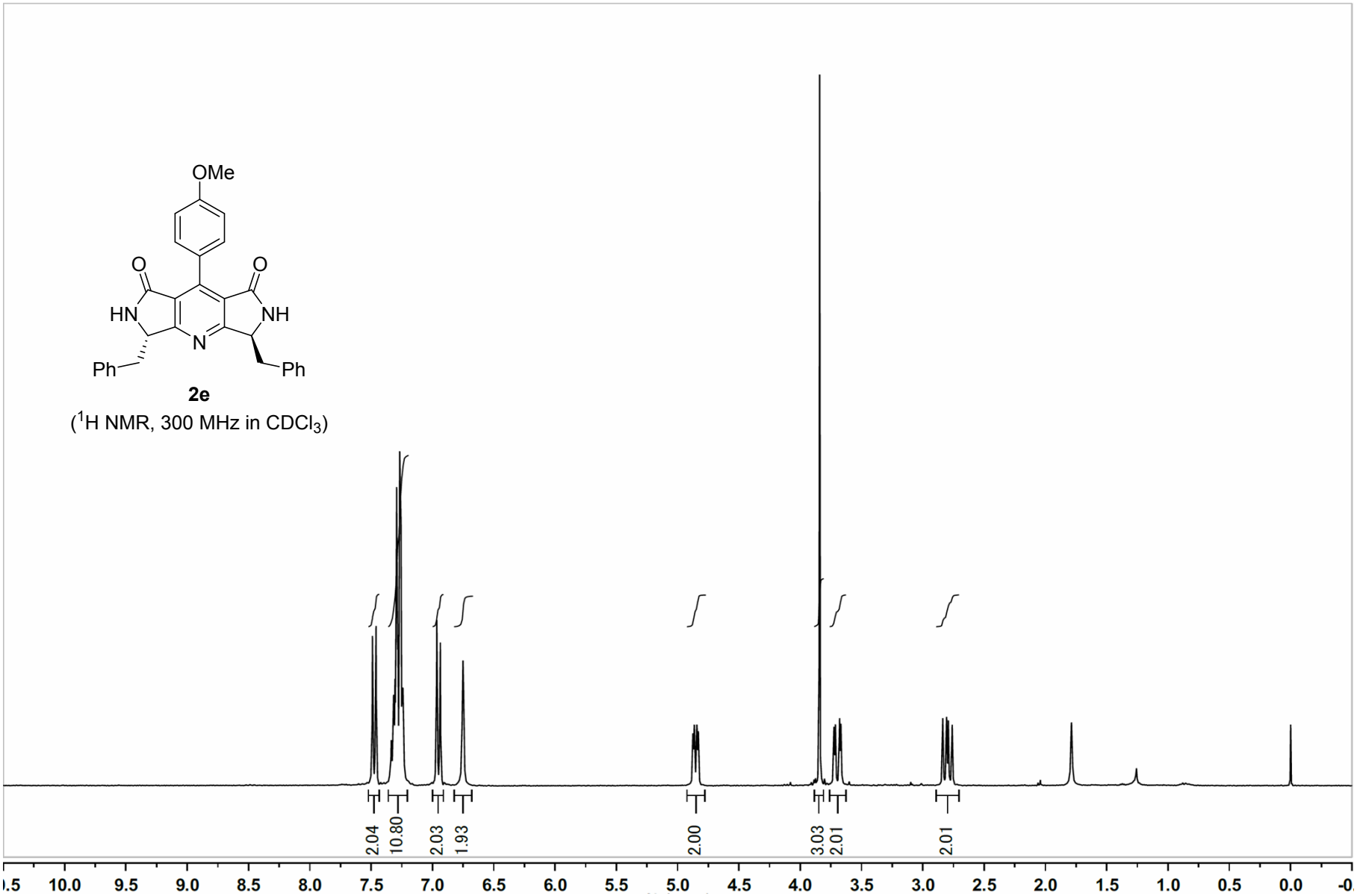

O
O
HN
NH
N
Ph
Ph
2c
(13C NMR, 75 MHz in CDCl3)
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1

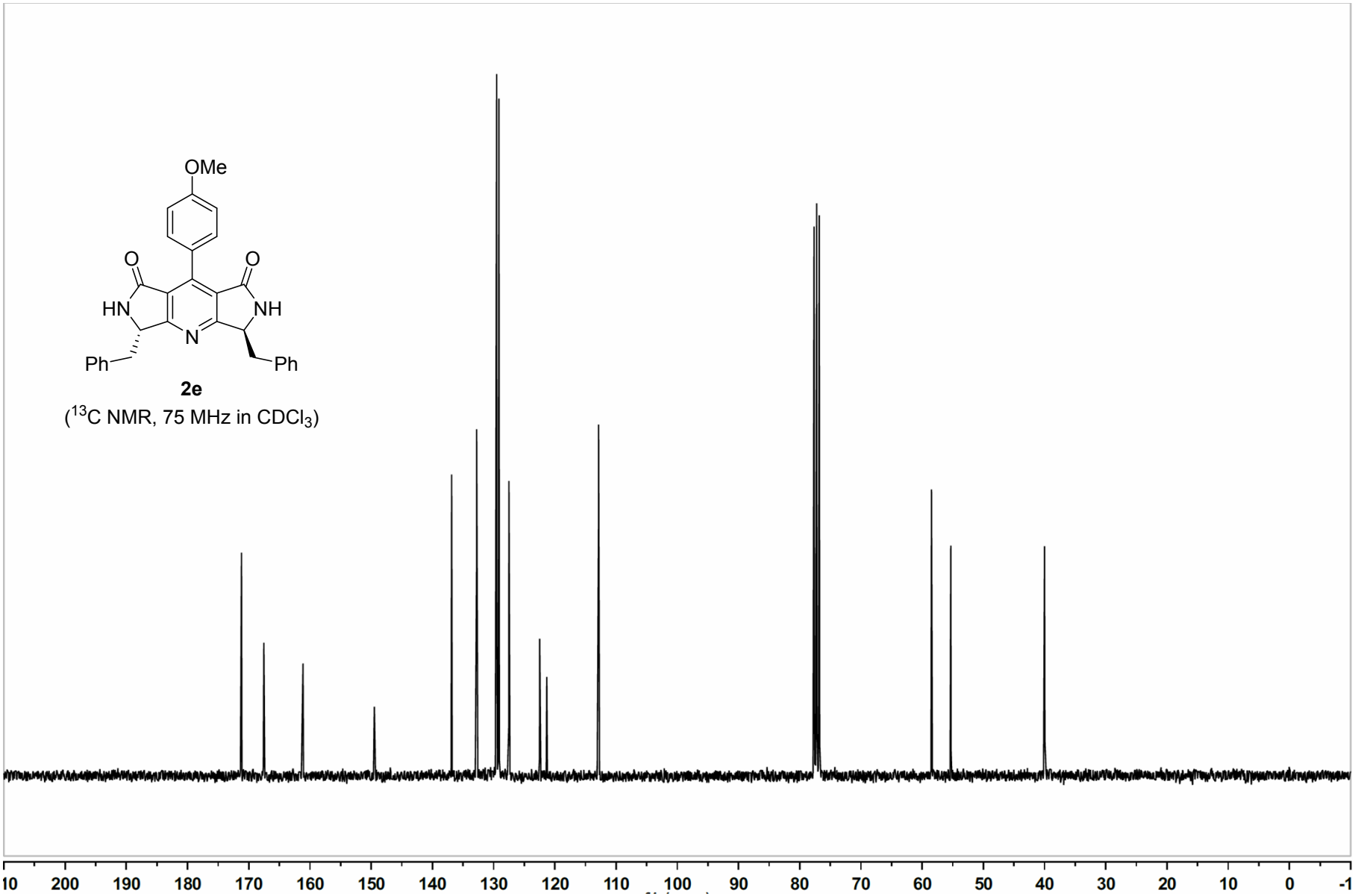


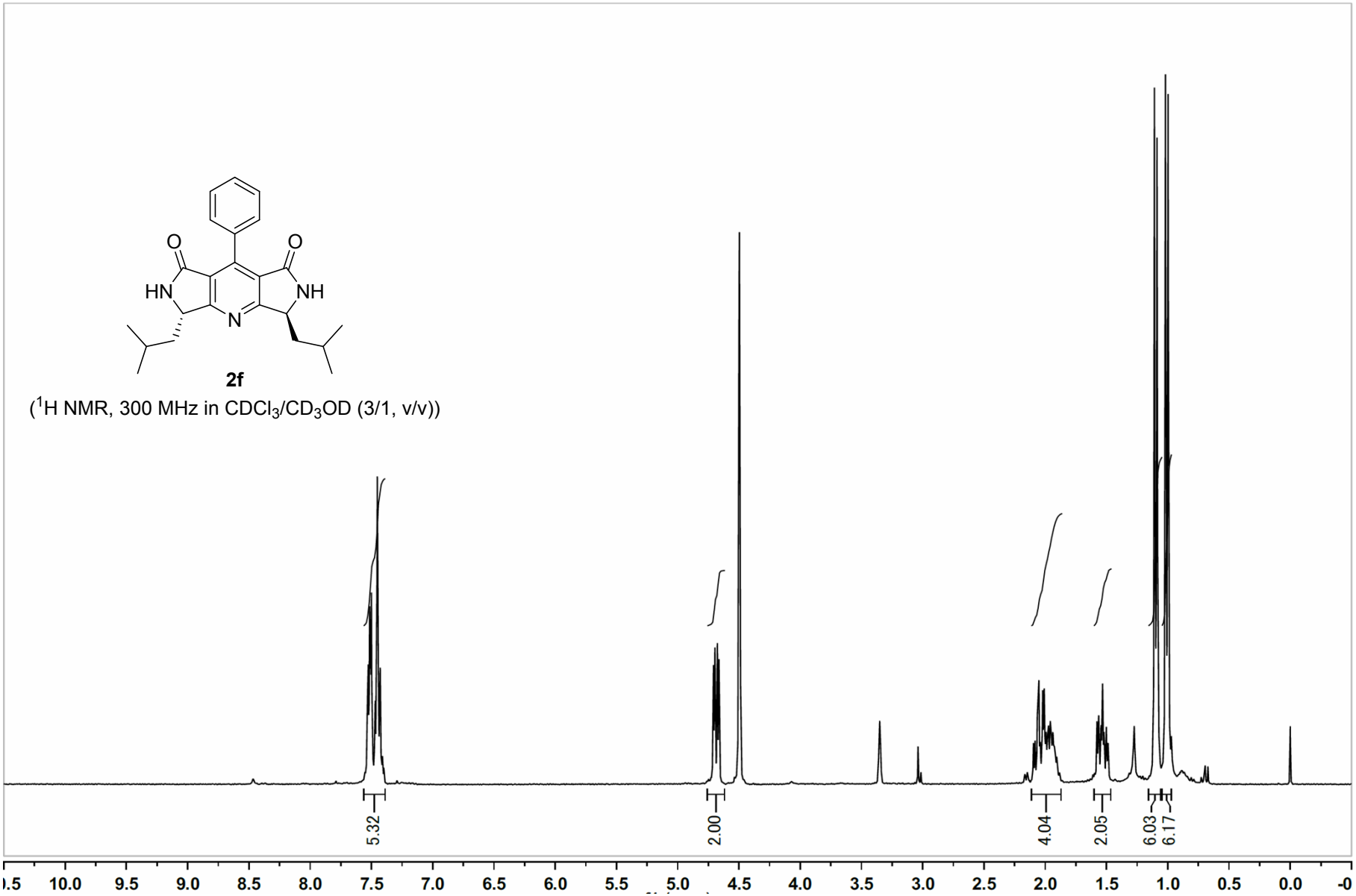
2d

(^{1}H NMR, 300 MHz in $CDCl_3$)


O
O
HN
NH
N
Ph
Ph
2d
(13C NMR, 75 MHz in CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

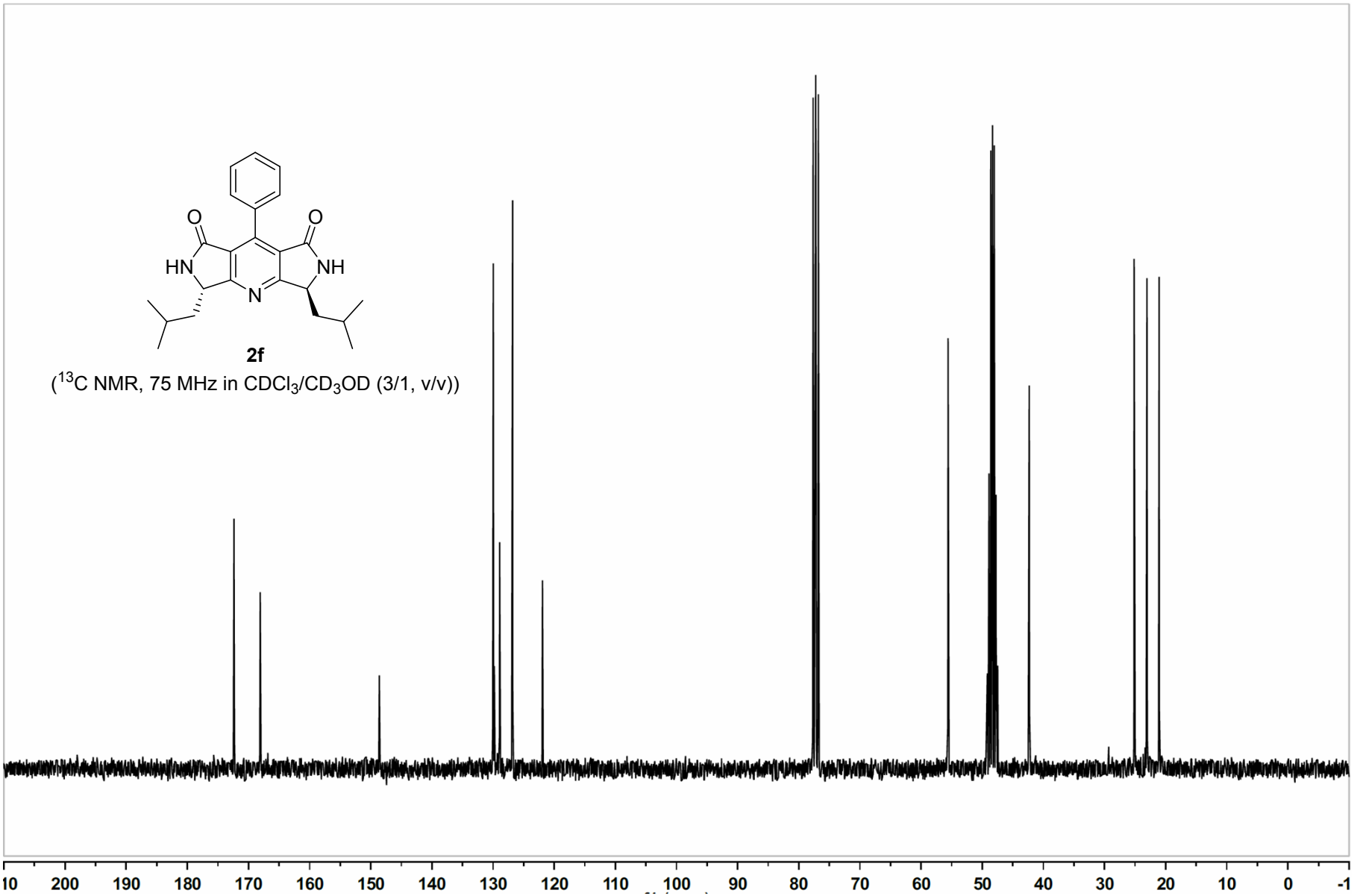

OMe
O
O
HN
NH
N
Ph
Ph
2e
(1H NMR, 300 MHz in CDCl3)
2.04
10.80
2.03
1.93
2.00
3.03
2.01
2.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

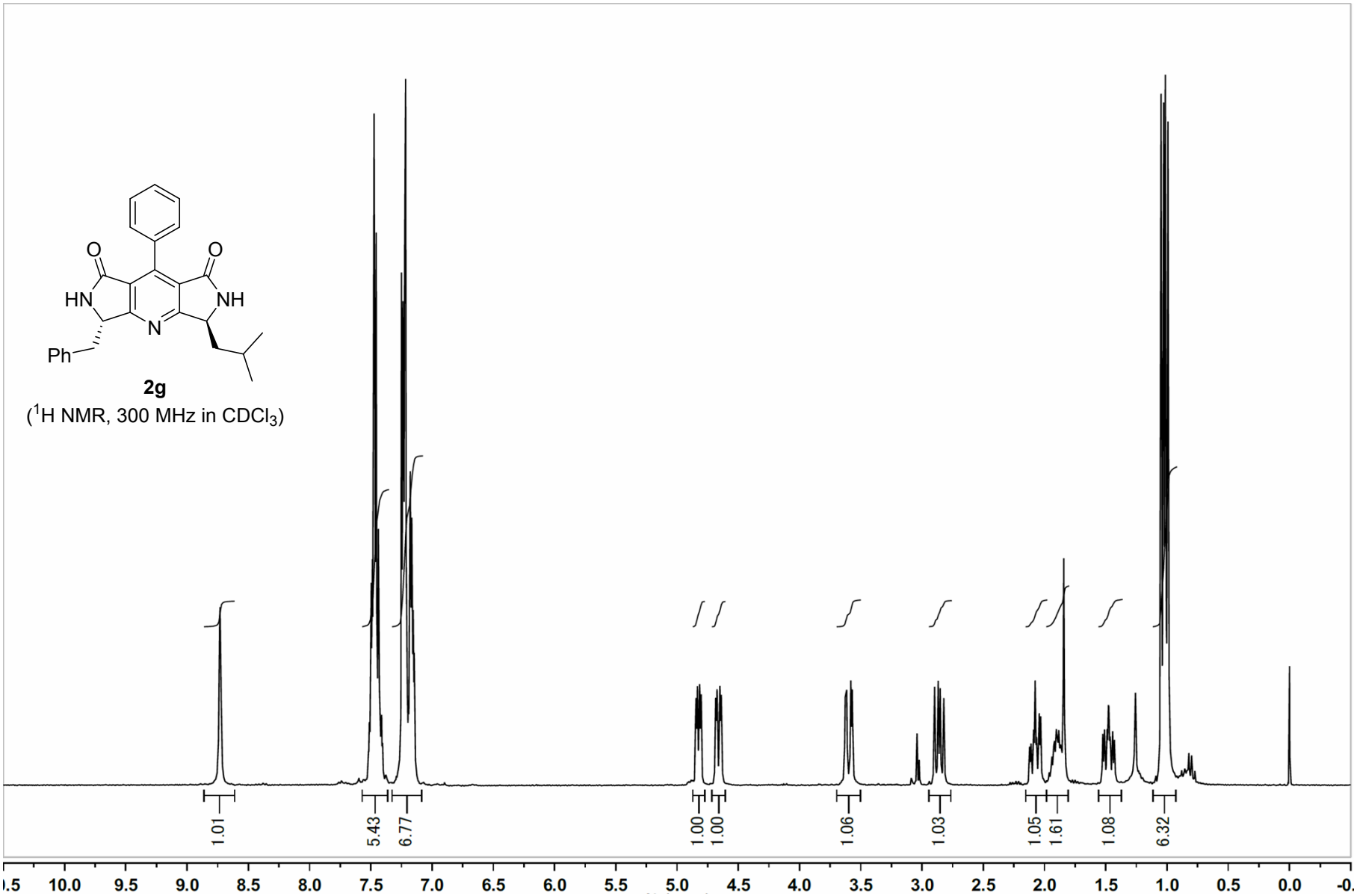

OMe
O
O
HN
NH
N
Ph
Ph
2e
(13C NMR, 75 MHz in CDCl3)
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1



2f

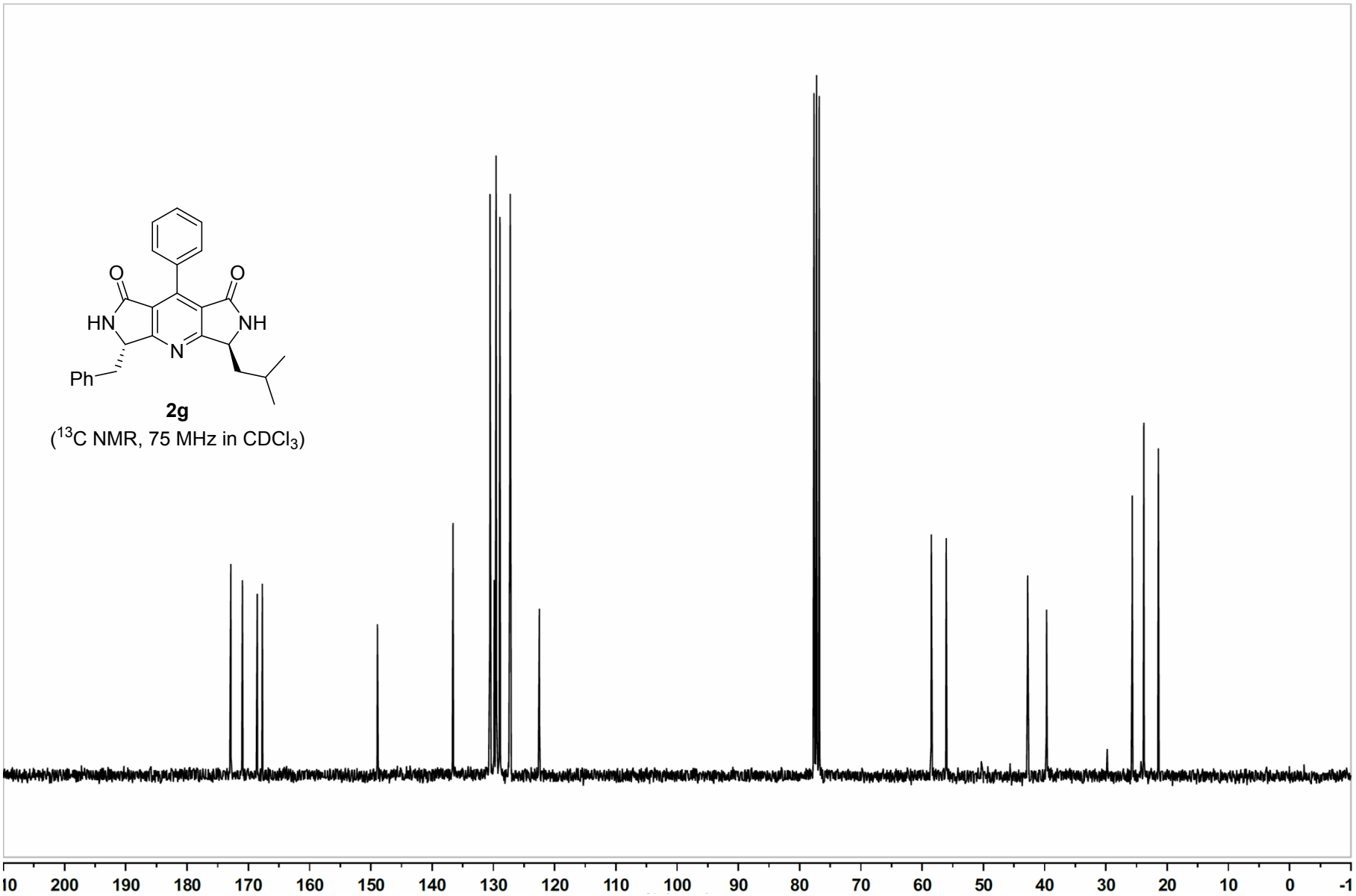
(^{1}H NMR, 300 MHz in $CDCl_3/CD_3OD$ (3/1, v/v))

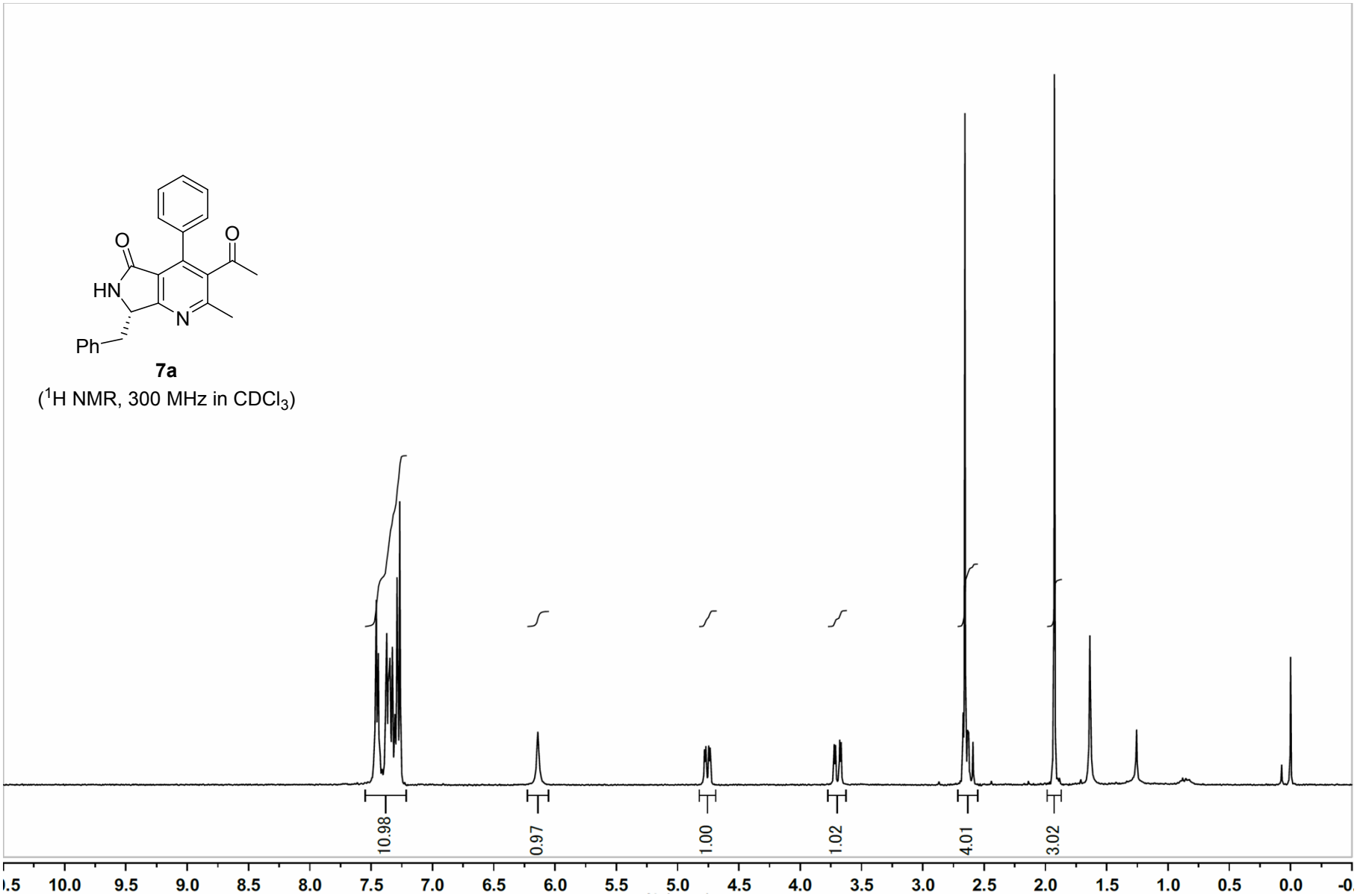

O
O
HN
NH
N
2f
(13C NMR, 75 MHz in CDCl3/CD3OD (3/1, v/v))
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1



2g

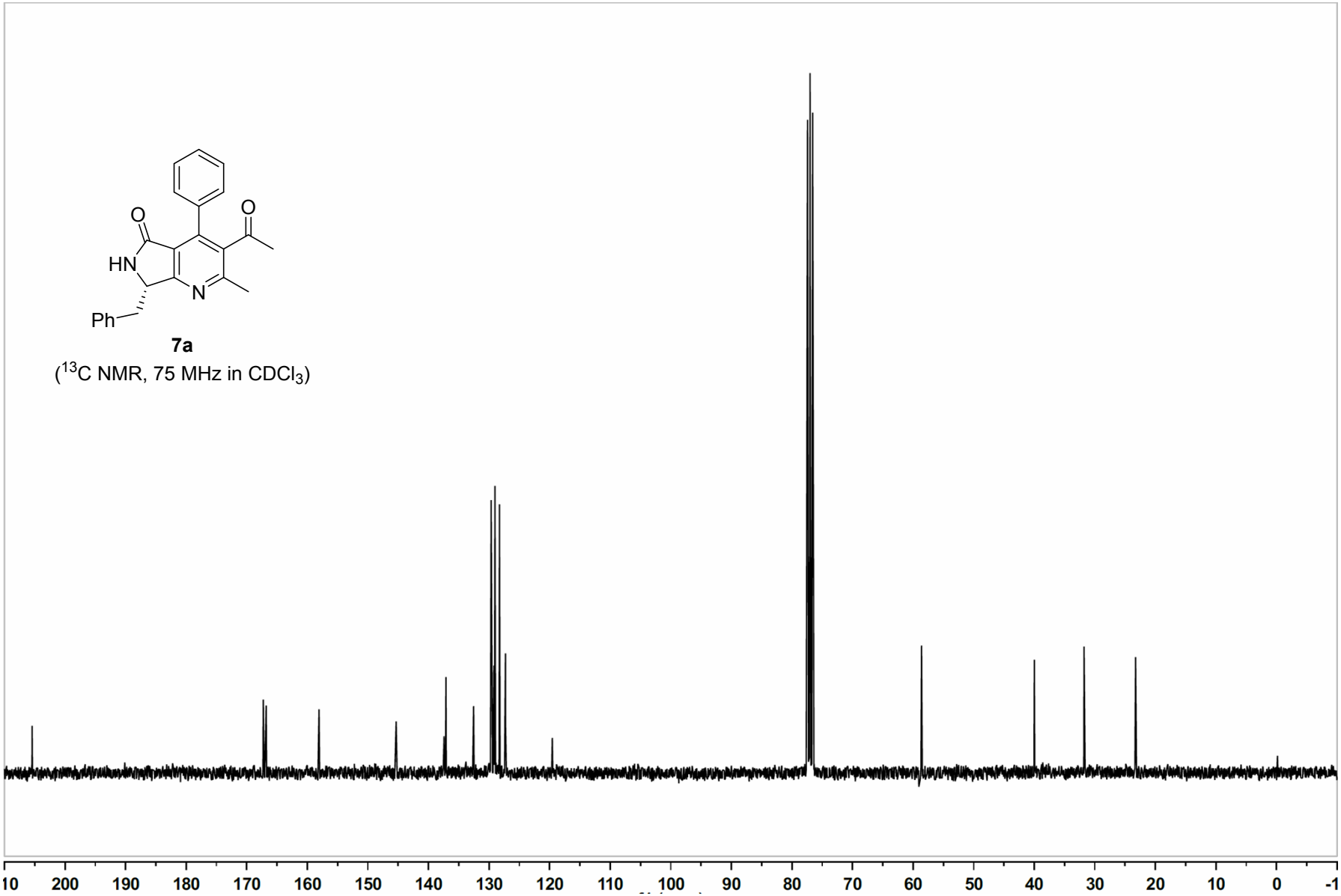
(^{1}H NMR, 300 MHz in $CDCl_3$)


O
O
HN
NH
N
Ph
2g
(13C NMR, 75 MHz in CDCl3)
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1



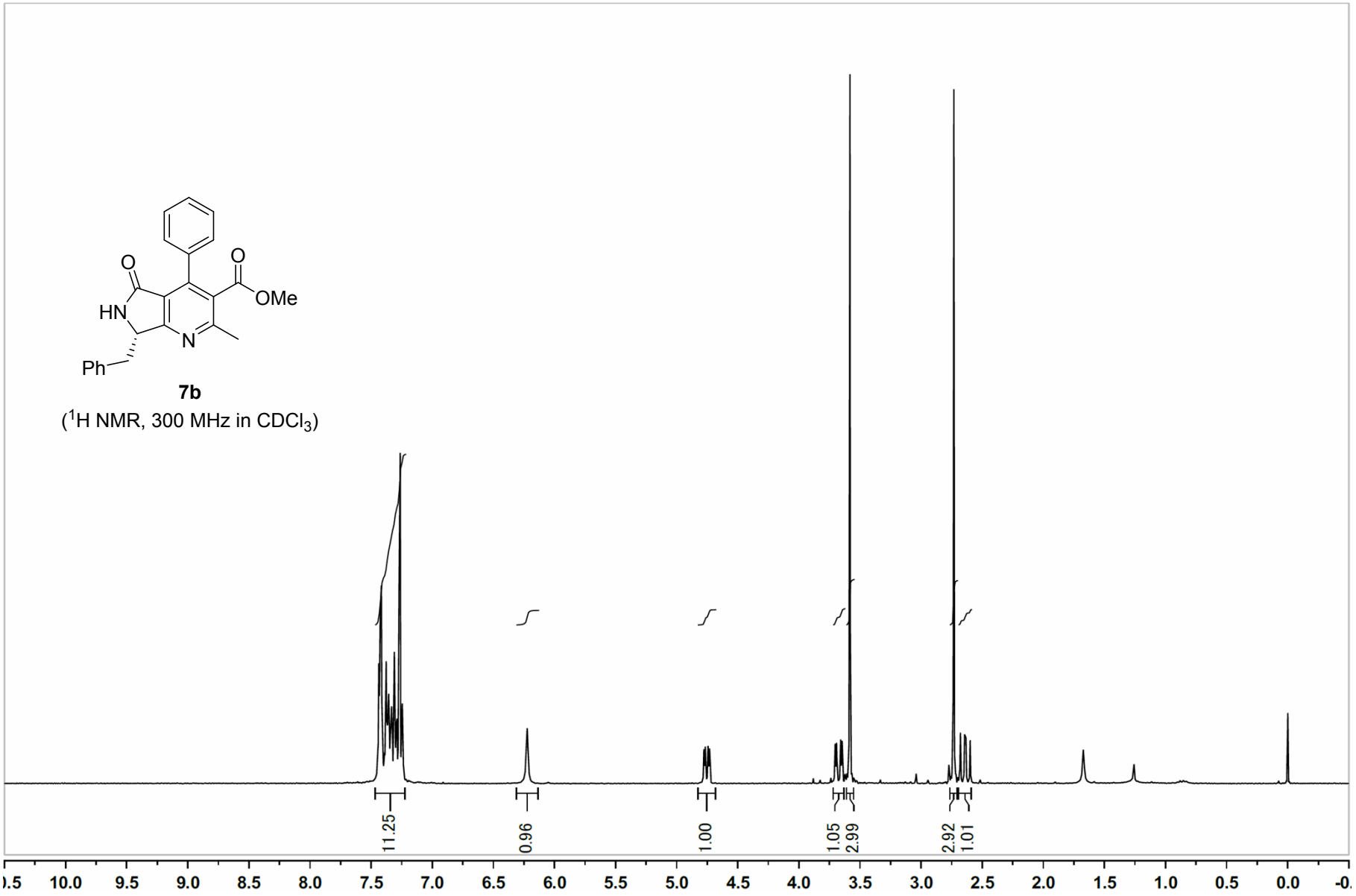
7a

(^{1}H NMR, 300 MHz in $CDCl_3$)



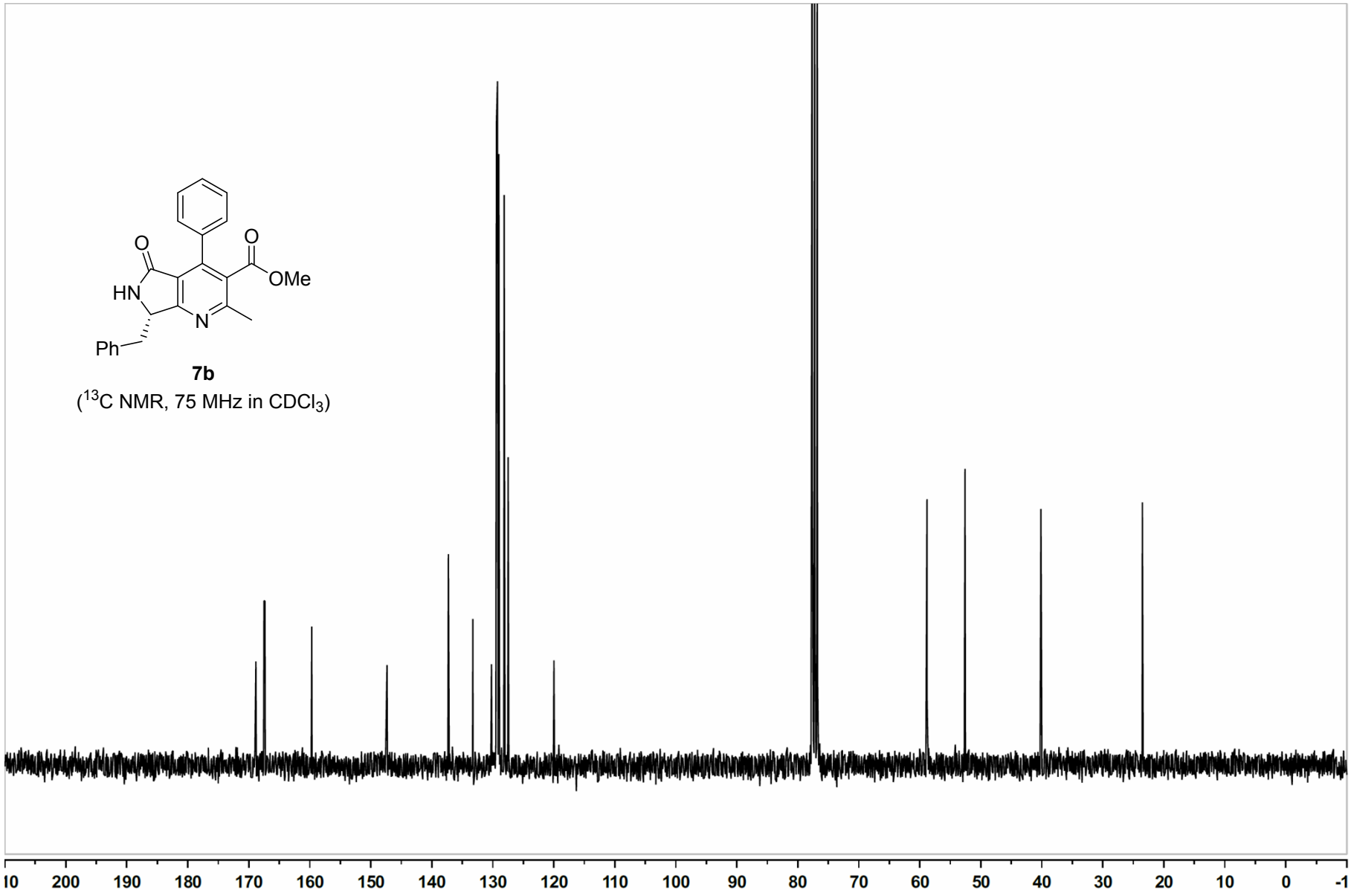
7a

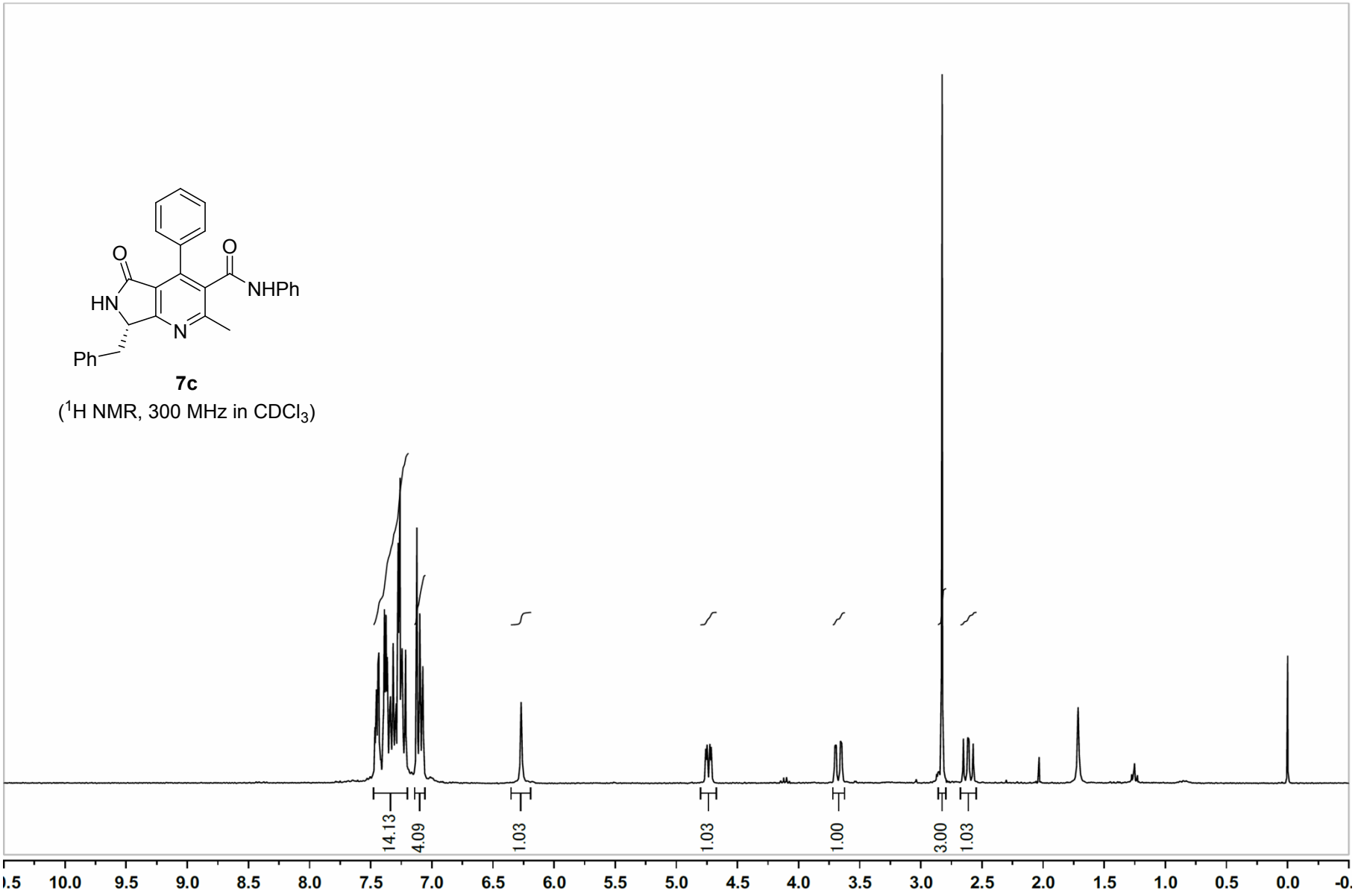
(^{13}C NMR, 75 MHz in $CDCl_3$)



7b

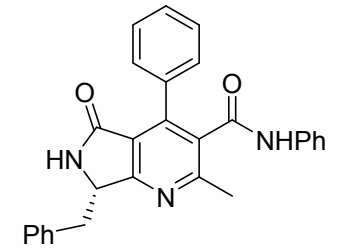
(^{1}H NMR, 300 MHz in $CDCl_3$)


O
O
OMe
HN
N
Ph
7b
(13C NMR, 75 MHz in CDCl3)
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1



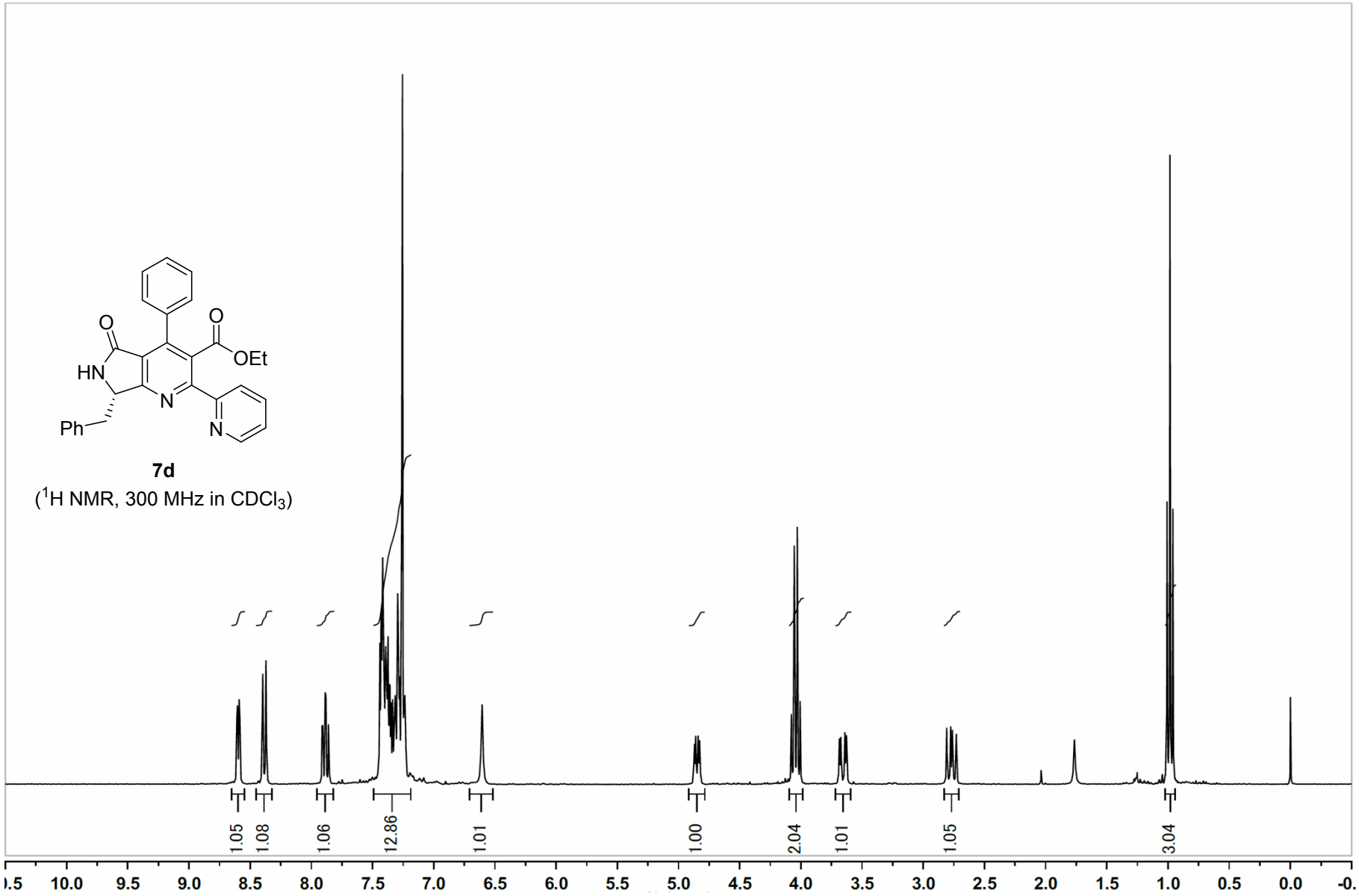
7c

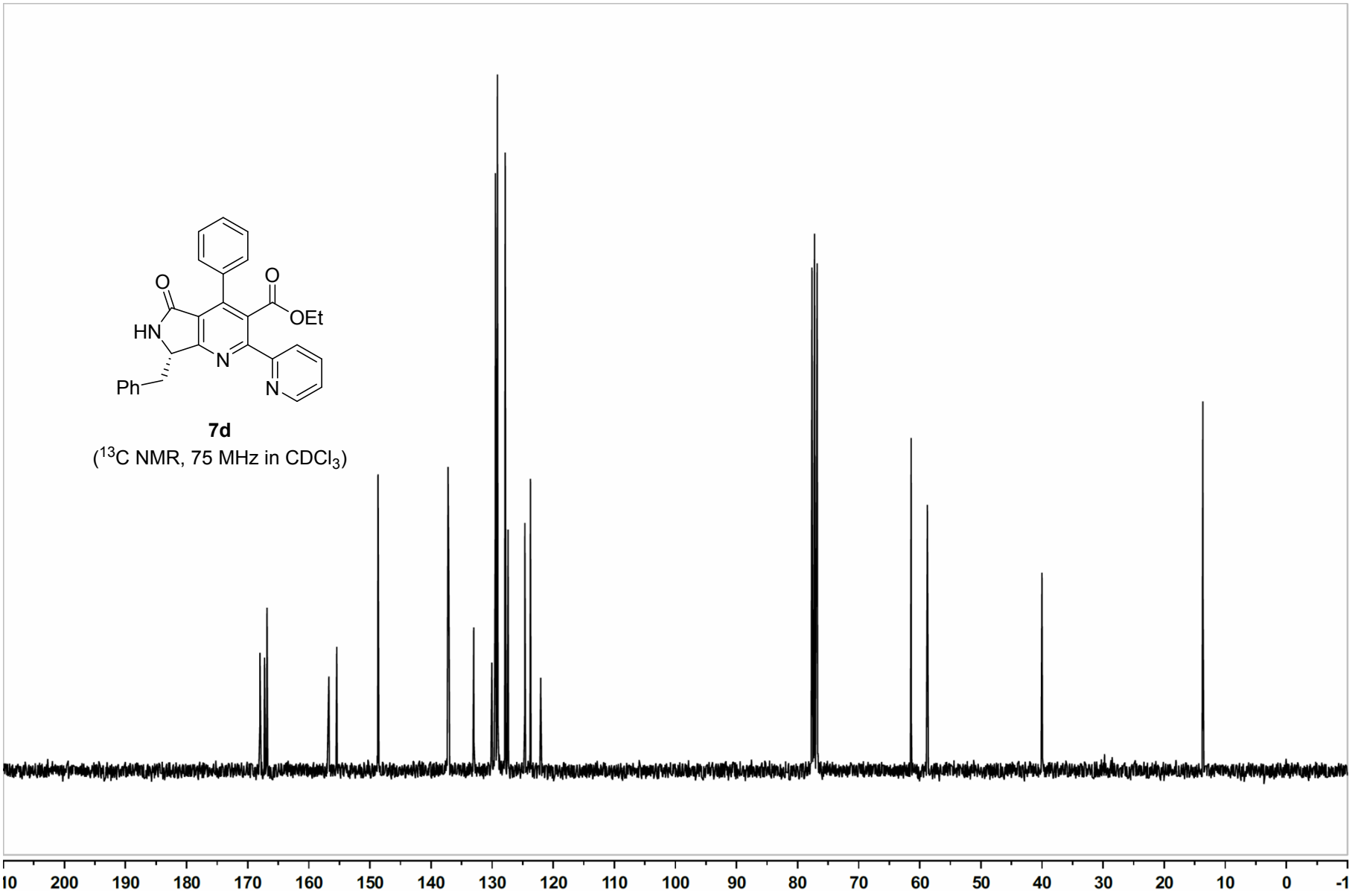
(^{1}H NMR, 300 MHz in $CDCl_3$)



7c

(^{13}C NMR, 75 MHz in $CDCl_3$)


O
O
OEt
HN
N
Ph
N
7d
(1H NMR, 300 MHz in CDCl3)
1.05
1.08
1.06
12.86
1.01
1.00
2.04
1.01
1.05
3.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


O
O
OEt
HN
N
Ph
N
7d
(^{13}C NMR, 75 MHz in $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10